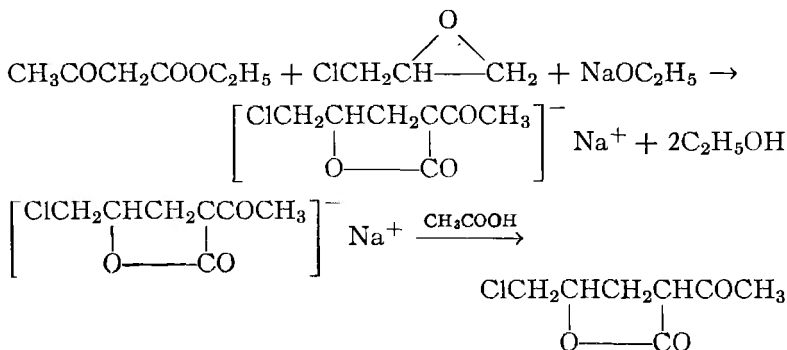


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α -ACETYL- δ -CHLORO- γ -VALEROLACTONE

(Valeric acid, α -acetyl- δ -chloro- γ -hydroxy-, γ -lactone)



Submitted by G. D. ZUIDEMA, E. VAN TAMELEN, and G. VAN ZYL.¹

Checked by WILLIAM S. JOHNSON and HERBERT I. HADLER.

1. Procedure

A 1-l. three-necked round-bottomed flask is equipped with a sealed stirrer, a thermometer, a dropping funnel, and an efficient condenser, the upper end of which is protected with a calcium chloride drying tube. In this flask 23 g. (1 gram atom) of lustrous metallic sodium (Note 1) is dissolved in 400 ml. of absolute ethanol (Note 2). The sodium is cut into about 25 pieces, and the entire amount is added at one time. It may be necessary to cool the flask in a cold-water bath if the reaction becomes violent. When all the sodium has dissolved, the solution is cooled to 50° and 130 g. (127 ml., 1 mole) of ethyl acetoacetate (Note 3) is added dropwise while the temperature is maintained between 45° and 50°. The resulting solution is cooled to about 35°, and 92.5 g. (78.4 ml., 1 mole) of epichlorohydrin (Note 4) is added dropwise with stirring over a period of 20 minutes. The temperature is then raised to 45° and is kept at 45–50° for 18 hours.

The clear red-orange solution is cooled to 15°, and chilled glacial acetic acid (60–65 ml.) is added with stirring until the solution is just acid to litmus; a mush of sodium acetate crystals precipitates. The dropping funnel is replaced by a capillary tube, and the condenser is set for distillation. About three-fourths of the ethanol is removed under reduced pressure while air is bubbled into the mixture through the capillary tube (Note 5). Care is taken that the internal temperature does not exceed 100°.

The mushy residue is shaken with 250–300 ml. of water until the sodium acetate dissolves. The oily layer of lactone is separated, and the aqueous phase is extracted with two 100-ml. portions of ether. The combined oil and ether extracts are washed with 150 ml. of water and dried overnight over anhydrous sodium sulfate. The ether is removed under reduced pressure, and the product is distilled from a modified Claisen flask. The fraction boiling at 160–170°/11 mm. is collected; refractionation yields 107–114 g. (61–64%) of product boiling at 164–168°/11 mm. or 151–156°/8 mm.; n_D^{25} 1.4815–1.4830 (Notes 6 and 7).

2. Notes

1. The sodium must be present in an equivalent amount for best results. When 0.2 gram atom of sodium was used, the yield was only 10%.

2. It is necessary to maintain strictly anhydrous conditions in this reaction. The apparatus should be carefully predried and the absolute ethanol freshly prepared either by the diethyl phthalate method² or by the magnesium ethoxide method.³

3. Eastman Kodak Company white label quality ethyl acetoacetate (b.p. 78–79°/11 mm.) was used.

4. Epichlorohydrin may be prepared from glycerol- α,γ -dichlorohydrin.⁴ It is also commercially available.

5. Unless this precaution is taken, there is considerable bumping due to the presence of the solid sodium acetate in the mixture.

6. The product may become slightly colored upon standing.

7. This reaction is typical of those between the following epoxides and ethyl acetoacetate:

EPOXIDE	BOILING POINT OF PRODUCT	% YIELD OF PRODUCT
Butadiene monoxide	148–151°/32 mm.	54
Propylene oxide	138–141°/26 mm.	49
Styrene oxide	164–167°/3 mm.	60
Ethyl glycidyl ether	160–163°/14–15 mm.	46
Phenyl glycidyl ether	195–197°/1 mm.	77

3. Method of Preparation

α -Acetyl- δ -chloro- γ -valerolactone has been prepared only by the condensation of epichlorohydrin with ethyl acetoacetate. The preparation described is based on the method of Traube and Lehman.⁵

¹ Hope College, Holland, Michigan.

² Manske, *J. Am. Chem. Soc.*, **53**, 1106 (1931), footnote 9.

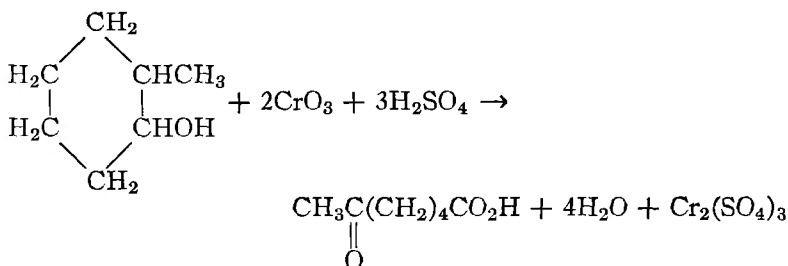
³ Lund and Bjerrum, *Ber.*, **64**, 210 (1931). See Fieser, *Experiments in Organic Chemistry*, 2nd ed., p. 359, D. C. Heath and Company, Boston, Massachusetts, 1941.

⁴ *Org. Syntheses* Coll. Vol. 1, 233 (1941).

⁵ Traube and Lehman, *Ber.*, **34**, 1980 (1901).

δ -ACETYL-*n*-VALERIC ACID

(Enanthic acid, ϵ -oxo-)



Submitted by J. R. SCHAEFFER and A. O. SNODDY.¹

Checked by RICHARD T. ARNOLD and H. W. TURNER.

1. Procedure

A solution of 368 g. of 96% sulfuric acid in 664 ml. of water is cooled to room temperature and placed in a 3-l. three-necked

flask provided with a mechanical stirrer, a thermometer, and a dropping funnel. To this acid solution is added 114 g. (1 mole) of 2-methylcyclohexanol (Note 1). A mixture of 220 g. (2.2 moles) of chromic oxide (Note 2) in 368 g. of 96% sulfuric acid and 664 ml. of water is added from the dropping funnel into the 2-methylcyclohexanol suspension at such a rate that the temperature of the mixture remains at $30 \pm 2^\circ$ (Note 3). Good agitation and an ice bath are necessary to control the temperature in this range. The mixture is stirred at $30 \pm 2^\circ$ for 1 hour and then at room temperature until all the chromic oxide is consumed (Note 4). The sulfuric acid solution is extracted with ether until the returns from the ether extractions fall to an insignificant amount. Approximately 10 extractions with 200-ml. portions of ether are required (Note 5). The ether extracts are combined, and the ether is removed by distillation on the steam bath. The resulting crude δ -acetyl-*n*-valeric acid is a yellow liquid with a sharp odor and amounts to about 130 g. The crude acid is purified by distillation through a 30-in. Vigreux column, using a variable take-off, a reflux ratio of 3:1, and a pressure of 1 mm. A fore-run of approximately 30 g. of material distilling up to $122^\circ/1$ mm. is obtained. The main fraction which distills at 122 – $123^\circ/1$ mm. is pure δ -acetyl-*n*-valeric acid and amounts to 66–79 g. (45–55%). The pure acid is a colorless crystalline hygroscopic solid which melts (sealed capillary) at 34 – 35° and is miscible with water in all proportions. The literature records the melting point of δ -acetyl-*n*-valeric acid as ranging from 31° to 42° .^{2,3,4}

2. Notes

1. Eastman Kodak Company practical grade 2-methylcyclohexanol was used in this preparation.

2. Technical grade chromic oxide (99.5% CrO_3) in flake form was used.

3. An alcohol-Dry Ice bath is very convenient for this purpose; with this bath only about 45 minutes is needed for the addition of the chromic oxide solution. A water-ice bath can be used, but a

longer time will be required for the addition of the chromic oxide solution.

4. The chromic oxide content of the mixture at any time may be determined by titrating a test portion against standard ferrous ammonium sulfate solution. If the mixture is allowed to stand overnight at room temperature without stirring, it will be free from chromic oxide. A convenient procedure is to perform the oxidation in the afternoon and the extraction the next day.

5. A liquid-liquid continuous extractor is convenient for extracting the crude acid from the aqueous solution. With such apparatus, it is possible to extract all the crude δ -acetyl-*n*-valeric acid from the aqueous acid in 6–8 hours.

6. The fore-run and the still residue contain some δ -acetyl-*n*-valeric acid. These fractions may be combined and redistilled to yield an additional 5–10% of δ -acetyl-*n*-valeric acid, but the low cost of the starting materials and the ease of preparing the crude δ -acetyl-*n*-valeric acid scarcely justify the labor unless a considerable number of batches are being prepared.

3. Methods of Preparation

δ -Acetyl-*n*-valeric acid has been prepared by the oxidation of 1-methylcyclohexene with potassium permanganate; ⁵ by the oxidation of 2-methylcyclohexanone with chromic oxide and sulfuric acid; ⁶ by the reaction of methylzinc iodide on the ethyl ester of adipic acid chloride and saponification of the ethyl ester of δ -acetyl-*n*-valeric acid so obtained; ⁷ by the saponification of the ethyl ester of diacetylvaleric acid; ² and through the hydrolysis of ethyl α -acetyl- δ -cyanovaleate with boiling 20% hydrochloric acid.³

¹ Procter and Gamble Company, Ivorydale, Ohio.

² Perkin, *J. Chem. Soc.*, **57**, 229 (1890).

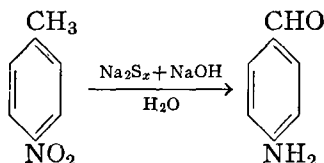
³ Derick and Hess, *J. Am. Chem. Soc.*, **40**, 551 (1918).

⁴ Blaise and Kohler, *Compt. rend.*, **148**, 490 (1909).

⁵ Wallach, *Ann.*, **329**, 371, 376 (1903).

⁶ Wallach, *Ann.*, **359**, 300 (1908).

⁷ Blaise and Kohler, *Bull. soc. chim.*, [4] **7**, 222 (1910).

***p*-AMINOBENZALDEHYDE**(Benzaldehyde, *p*-amino-)Submitted by E. CAMPAIGNE, W. M. BUDDE, and G. F. SCHAEFER.¹

Checked by CLIFF S. HAMILTON and R. C. RUPERT.

1. Procedure

To 600 ml. of distilled water in a 1-l. beaker are added 30 g. (0.125 mole) of crystalline sodium sulfide nonahydrate (Note 1), 15 g. (0.47 gram atom) of flowers of sulfur, and 27 g. (0.67 mole) of sodium hydroxide pellets. The mixture is heated on a steam bath for 15–20 minutes with occasional stirring and then poured into a 2-l. round-bottomed flask containing a hot solution of 50 g. (0.36 mole) of *p*-nitrotoluene (Note 2) in 300 ml. of 95% ethanol. A reflux condenser is attached, and the mixture is heated under reflux for 3 hours. The resulting clear but deep red solution is rapidly steam-distilled until about 1.5–2 l. of condensate has been collected (Note 3). The distillate should be clear when the distillation is stopped. The residue in the 2-l. flask should have a volume of 500–600 ml.; if less, it should be diluted to this volume with boiling water. The solution is rapidly chilled in an ice bath with occasional vigorous shaking and stirring to induce crystallization. After 2 hours in the ice bath the golden yellow crystals of *p*-aminobenzaldehyde are collected on a Büchner funnel and washed with 500 ml. of ice water to remove sodium hydroxide (Note 4). The product is immediately placed in a vacuum desiccator over solid potassium hydroxide pellets for 24 hours. The yield of *p*-aminobenzaldehyde, m.p. 68–70°, amounts to 18–22 g. (40–50%). The product

contains some impurities but is pure enough for most purposes (Note 5). It should be stored in a sealed bottle (Note 6).

2. Notes

1. Merck's reagent grade of sodium sulfide nonahydrate was used. Since sodium sulfide decomposes on contact with air, a freshly opened bottle should be employed. "Sodium Sulphydrate" (Hooker Electrochemical Company hydrated sodium hydrosulfide) is also satisfactory; the amount should be based upon the formula $\text{NaHS} \cdot 2\text{H}_2\text{O}$, and an equivalent amount of sodium hydroxide in excess of the 27 g. is required.

2. The *p*-nitrotoluene used was Eastman Kodak Company practical grade.

3. The steam distillation should be carried out as rapidly as possible. The distillate contains ethanol, *p*-toluidine, and some unchanged *p*-nitrotoluene.

4. It is sometimes necessary to suspend the precipitate in about 200 ml. of ice water, stir it vigorously, and filter again to remove all traces of alkali.

5. The chief impurities are the polymeric condensation products of *p*-aminobenzaldehyde with itself. No satisfactory method for recrystallization has been found. If the melting point is high and a pure product is desired, it is best to extract with boiling water until the filtrate is clear, and extract the monomer from the water with ether. This procedure gives recoveries of 25–30%.

Readily purified aldehyde derivatives may be prepared in good yield from the crude polymer mixture. The oxime melts at 124°, the hydrazone at 245°, and the phenylhydrazone² at 175°. If these derivatives are hydrolyzed the same crude *p*-aminobenzaldehyde of broad melting range results.

6. Care must be taken to exclude all traces of acid fumes from *p*-aminobenzaldehyde, since they catalyze its self-condensation.

3. Methods of Preparation

p-Aminobenzaldehyde has been prepared by the action of sodium polysulfide upon *p*-nitrotoluene,^{3,4} on which the method described is based.

It can also be prepared from *p*-nitrobenzyl alcohol and sodium sulfide,⁴ by heating *p*-nitrobenzaldehyde with sodium bisulfite⁵ and decomposing the addition product with hydrochloric acid, or in low yield by the reduction of *p*-nitrobenzaldoxime with ammonium sulfide^{6,7} and subsequent acid hydrolysis of the amino oxime.

¹ Indiana University, Bloomington, Indiana.

² Walther and Kausch, *J. prakt. Chem.*, [2] **56**, 97 (1897).

³ Geigy, Ger. pat. 86,874 (1895) [*Frdl.*, **4**, 136 (1894-1897)]; Friedlander and Lenk, *Ber.*, **45**, 2087 (1912).

⁴ Beard and Hodgson, *J. Chem. Soc.*, **1944**, 4.

⁵ Meister, Lucius, and Brünig, Ger. pat. 106,590 (1898) [*Chem. Centr.*, I **71**, 1084 (1900)].

⁶ Cohn and Springer, *Monatsh.*, **24**, 87 (1903).

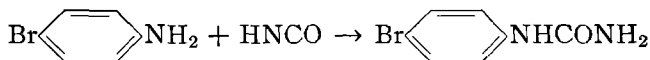
⁷ Gabriel and Herzberg, *Ber.*, **16**, 2000 (1883).

ARYLUREAS

I. CYANATE METHOD

p-BROMOPHENYLUREA

[Urea, 1-(*p*-bromophenyl)-]



Submitted by FREDERICK KURZER.¹

Checked by RICHARD T. ARNOLD and LESTER C. KROGH.

1. Procedure

In a 2-l. beaker, 86 g. (0.5 mole) of *p*-bromoaniline is dissolved in 240 ml. of glacial acetic acid and 480 ml. of water at 35°. This solution is treated with a solution of 65 g. (1 mole) of sodium cyanate (Note 1) in 450 ml. of water at 35° (Note 2). About 50 ml. of the sodium cyanate solution is added slowly with stirring

until a white crystalline precipitate of the product appears. The rest is then added quickly with vigorous agitation (Note 3). The very rapid separation of the product is accompanied by a rise in the temperature to 50–55°. The thick, paste-like suspension is stirred for another 10 minutes, allowed to stand at room temperature for 2–3 hours, and diluted with 200 ml. of water. After cooling to 0°, the material is filtered with suction, washed with water, drained thoroughly, and dried. The yield of crude *p*-bromophenylurea, a white crystalline powder, is 95–100 g. (88–92%). The product is sufficiently pure for further synthetic work, but it can be recrystallized from aqueous ethanol (12 ml. of ethanol and 3 ml. of water per gram of crude material) to give a 65% recovery of lustrous white prisms of *p*-bromophenylurea, m.p. 225–227° (Note 4). This method is suitable for the preparation in excellent yields of a large number of arylureas (Note 5).

2. Notes

1. Comparable results are obtained with an equivalent quantity (81 g.) of potassium cyanate.

2. Instead of the solution, a well-stirred suspension of the cyanate in 150 ml. of water may be used with equal success.

3. Considerable frothing occurs with loss of some isocyanic acid (faint smell resembling that of sulfur dioxide). The foam collapses readily on stirring.

4. Melting points varying between 220° and 278° have been reported for *p*-bromophenylurea (see Methods of Preparation). It has been shown² that the thermal conversion of arylureas to the corresponding diarylureas takes place extremely rapidly, even below the melting point. This is particularly true of arylureas containing certain substituents in the *para* position to the ureido grouping. Melting points of such compounds are therefore liable to be indefinite and correspond to mixtures of the *mono* and *sym.* disubstituted urea, especially if the temperature is raised slowly.

Reproducible values for the melting points of such compounds, including *p*-bromophenylurea, have now been determined by the following simple procedure: After the approximate softening

temperature or melting range of the urea derivative has been found, the bath temperature of the apparatus is raised a further 10–20° above that point and samples are inserted into the slowly cooling bath until a temperature is reached at which a specimen just fails to liquefy. Insertion of a further specimen at a temperature 1° higher causes instantaneous fusion and can be taken as the “melting point” of the urea derivative under examination. Under these conditions practically no conversion to a diarylurea occurs, and samples withdrawn immediately after fusion show nitrogen contents corresponding to the original arylurea. This method gives reproducible physical constants for urea derivatives whose properties preclude slow heating.

5. A list of substituted arylureas prepared by the above method is given in the table, which records slight variations in the quantities of starting materials employed and in the yields obtained.

The quantities of water recorded in column III are used for preparing the arylamine acetate solutions. The sodium cyanate is dissolved or suspended in the appropriate volume of water as detailed in the synthesis of *p*-bromophenylurea. The yields refer to the quantity of crude product. The substituted ureas thus obtained are usually sufficiently pure for further syntheses but can be recrystallized from ethanol.

SUBSTITUTED ARYLUREAS

I	II	III	IV	V	VI	VII
Arylurea	Aryl- amine, mole	Water, ml.	Acetic Acid, ml.	Sodium Cyanate, mole	Initial Tempera- ture, °C	Yield, %
<i>p</i> -Tolylurea	0.5	500	50	1.0	25	96
<i>m</i> -Tolylurea	0.5	400	75	1.0	30	86
<i>o</i> -Tolylurea	0.5	400	75	1.0	30	94
1-(4-Biphenyl)urea	0.3	500	350	0.6	40	80
1-(2-Biphenyl)urea	0.25	400	400	0.5	30	75
<i>p</i> -Methoxyphenylurea	0.3	150	30	0.6	40	94
<i>p</i> -Ethoxyphenylurea	0.5	500	75	1.0	25	95
<i>m</i> -Ethoxyphenylurea	0.3	500	120	0.6	20	54
<i>o</i> -Ethoxyphenylurea	0.5	500	170	1.0	20	88
<i>m</i> -Bromophenylurea	0.5	300	150	1.0	20	90
<i>o</i> -Bromophenylurea	0.5	100	250	1.0	25	92
<i>o</i> -Chlorophenylurea	0.5	100	200	1.0	25	92

3. Methods of Preparation

p-Bromophenylurea has been prepared by the bromination of phenylurea, using glacial acetic acid,^{3,4} ethanol,⁴ or chloroform⁵ as solvents; by the action of potassium cyanate on *p*-bromoaniline hydrochloride;^{4,6} and by the interaction of *p*-bromoaniline and ethyl allophanate.⁷

¹ University of London, London, England.

² Kurzer, *J. Chem. Soc.*, **1949**, 2292.

³ Pinnow, *Ber.*, **24**, 4172 (1891).

⁴ Wheeler, *J. Am. Chem. Soc.*, **51**, 3653 (1929).

⁵ Desai, Hunter, and Khalidi, *J. Chem. Soc.*, **1934**, 1186.

⁶ Scott and Cohen, *J. Chem. Soc.*, **121**, 2034 (1922).

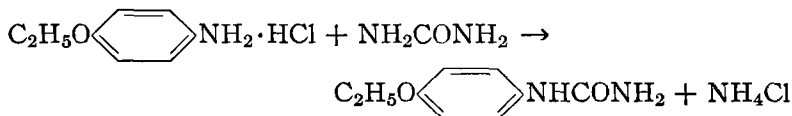
⁷ Dains and Wertheim, *J. Am. Chem. Soc.*, **42**, 2303 (1920).

II. UREA METHOD

p-ETHOXYPHENYLUREA

[Urea, 1-(*p*-phenetyl)-]

(Dulcin)



1. Procedure

A mixture of 870 g. (5 moles) of *p*-phenetidine hydrochloride and 1.2 kg. (20 moles) of urea is placed in a 12-l. round-bottomed flask (Note 1). To this mixture are added 2 l. of water, 40 ml. of concentrated hydrochloric acid, and 40 ml. of glacial acetic acid, and the well-shaken suspension is heated to boiling. The dark purple solution thus obtained is boiled vigorously for 45–90 minutes until the reaction is complete. The liquid remains clear during the first half of the heating period. Separation of the product begins during the last half and proceeds with increasing rapidity until the entire contents of the vessel suddenly set to a

solid mass. The source of heat is immediately withdrawn at this point (Note 2).

After cooling to room temperature, the mass of crude product is broken up with addition of 1-1.5 l. of water, filtered with suction, washed with cold water, drained, and dried. The crude *p*-ethoxyphenylurea is obtained in a yield of 740-810 g. (82-90%) as a nearly white to pale yellow solid (Note 3). This material may be purified by recrystallization from boiling water (Note 4), when minute white plates, m.p. 173-174°, are obtained. The method is applicable to the preparation of other substituted arylureas (Note 5).

2. Notes

1. An enameled-steel vessel of approximately 2-gal. capacity is suitable for carrying out this reaction.

2. After removal of the heat source, a vigorous reaction may continue for a few minutes, and the reaction mixture tends to froth somewhat. It eventually sets to a sponge-like formation of a crystalline mass. In smaller-scale experiments the final stage of the reaction is more easily controlled. The checkers employed one-tenth the scale and conventional equipment.

3. The crude product contains varying small quantities of the symmetrical disubstituted compound, di-(*p*-ethoxyphenyl)urea, [$(p\text{-C}_2\text{H}_5\text{OC}_6\text{H}_4\text{NH})_2\text{CO}$]. This substance is removed in the crystallization from water (Note 4).

4. To 1 l. of boiling water, 35 g. of crude *p*-ethoxyphenylurea is added. The bulk of the urea dissolves readily, and the solution is decolorized by the addition of 3 g. of activated charcoal, boiled for 5 minutes, and quickly filtered with suction through a pre-heated Büchner funnel. The colorless filtrate is slowly cooled to 0°, when lustrous minute plates of *p*-ethoxyphenylurea separate. An 80% recovery of material having a m.p. of 173-174° is obtained. Prolonged boiling of the solution should be avoided, since slow conversion to *sym.*-di-(*p*-ethoxyphenyl)urea occurs under these conditions.

5. *p*-Anisidine hydrochloride (0.5 mole), when boiled with the proportionate quantities of urea and other reagents for 1 hour,

gives 80–85% yields of *p*-methoxyphenylurea. Owing to the greater solubility of this product in water, less of the material separates during the heating period, but satisfactory crystallization occurs when the reaction liquid is slowly cooled to 0°. 1-Amino-2-naphthol hydrochloride gives 72–87% yields of 1-(2-hydroxy-1-naphthyl)urea.

3. Methods of Preparation

p-Ethoxyphenylurea has been prepared by the action of potassium cyanate on *p*-phenetidine hydrochloride¹ or *p*-phenetidine acetate,² and by the interaction of *p*-phenetidine with the following agents: phosgene in benzene or toluene and treatment of the product with ammonia;³ urethan;⁴ urea salts;⁵ acetylurea;⁶ and a mixture of urea and ammonium chloride.⁷ It has been obtained from the reaction of phenetidine salts (usually the hydrochloride) with urea,^{5, 8} or with a mixture of sodium cyanide and sodium hypochlorite or peroxide.⁹ *p*-Ethoxyphenylurea has also been prepared by heating *p*-ethoxyphenylurethan and ammonia to 100–180°;⁴ by heating di-(*p*-ethoxyphenyl)urea with urea, ammonium carbamate, commercial ammonium carbonate,¹⁰ or ethanol and ammonia;¹¹ by treating ammonium *p*-ethoxyphenyldithiocarbamate with lead carbonate in alcoholic solution;¹² by ethylating *p*-hydroxyphenylurea;¹³ and by the action of ammonia on *p*-ethoxyphenylisocyanate.¹⁴

¹ Berlinerblau, *J. prakt. Chem.*, [2] **30**, 103 (1884).

² Sonn, Ger. pat. 399,889 (1924) [*Chem. Centr.*, II **95**, 1513 (1924)].

³ Berlinerblau, Ger. pat. 63,485 [*Frld.*, **3**, 906 (1890–1894)].

⁴ Riedel, Ger. pat. 77,420 [*Frld.*, **4**, 1269 (1894–1897)].

⁵ Riedel, Ger. pat. 76,596 [*Frld.*, **4**, 1268 (1894–1897)].

⁶ Riedel, Ger. pat. 79,718 [*Frld.*, **4**, 1270 (1894–1897)]; Roy and Ray, *Quart. J. Indian Chem. Soc.*, **4**, 339 (1927).

⁷ Loginov and Polyanskii, U.S.S.R. pat. 65,779 [*C. A.*, **40**, 7234 (1946)].

⁸ Roura, *Industria y química Buenos Aires*, **3**, 160 (1941).

⁹ Riedel, Ger. pat. 313,965 [*Frld.*, **13**, 1049 (1916–1921)].

¹⁰ Riedel, Ger. pat. 73,083 [*Frld.*, **3**, 907 (1890–1894)].

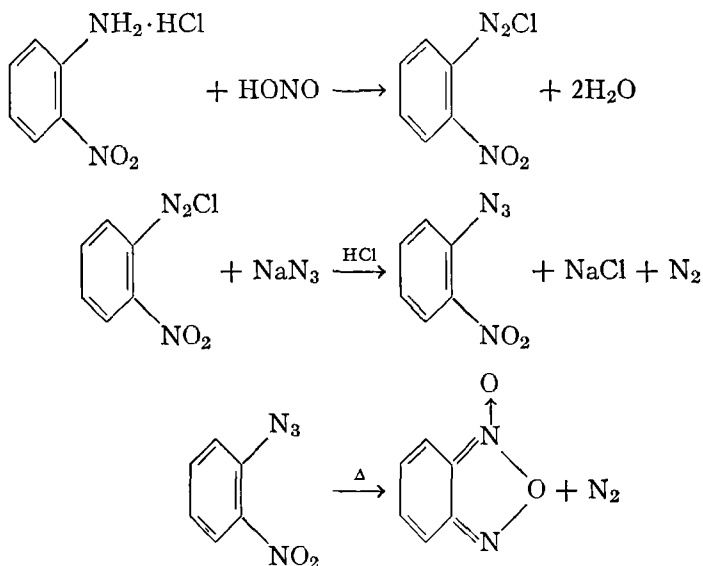
¹¹ Riedel, Ger. pat. 77,310 [*Frld.*, **4**, 1271 (1894–1897)].

¹² Heller and Bauer, *J. prakt. Chem.*, [2] **65**, 379 (1902).

¹³ Riedel, Ger. pat. 335,877 (1921) [*Chem. Centr.*, IV **92**, 1324 (1921)].

¹⁴ Sah and Chang, *Ber.*, **69**, 2762 (1936).

BENZOFURAZAN OXIDE



Submitted by P. A. S. SMITH and J. H. BOYER.¹

Checked by ARTHUR C. COPE, DAVID J. MARSHALL, and DOUGLAS S. SMITH.

1. Procedure

A. *o*-Nitrophenylazide. A mixture of 28 g. (0.2 mole) of *o*-nitroaniline (Note 1), 80 ml. of water, and 45 ml. of concentrated hydrochloric acid is placed in a 500-ml. three-necked flask equipped with a stirrer, a thermometer, and a dropping funnel. The stirrer is started, and the flask is cooled in an ice-salt bath until the temperature of the mixture is 0–5°. After this temperature has been reached, the amine hydrochloride is diazotized by adding dropwise a solution of 14.5 g. of reagent grade sodium nitrite in 50 ml. of water. Stirring is then continued for 1 hour at 0–5°. The yellow-green solution is filtered from traces of insoluble impurities and poured into a 2-l. beaker surrounded by an ice bath. With stirring, a solution of 13 g. (0.2 mole) of sodium azide in 50 ml. of water is added (Note 2). Almost

immediately the *o*-nitrophenylazide begins to precipitate as a light-cream to colorless solid, which is collected on a Büchner funnel after the nitrogen evolution has ceased (15–20 minutes). The yield of *o*-nitrophenylazide, m.p. 52–55°, is 31–32 g. (94–97%). This crude product can be used for the preparation of benzofurazan oxide in Part B (Note 3).

The impure azide is dissolved in 110–120 ml. of 95% ethanol at 50–55° (Note 4), and 2 g. of activated carbon is added to aid in the removal of impurities. After being filtered through a steam-heated funnel, the warm solution is allowed to cool to room temperature, whereupon 14–15 g. of the product precipitates as light-yellow prisms, m.p. 53–55°. Concentration (Note 5) of the mother liquor to 30–40 ml. by evaporation at room temperature under an air stream causes the separation of an additional 7–8 g. of material, m.p. 52–54° (Note 6). The total yield of purified *o*-nitrophenylazide is 63–69%.

B. Benzofurazan oxide. A mixture of 16.4 g. (0.1 mole) of *o*-nitrophenylazide and 30 ml. of reagent grade toluene is placed in a 100-ml. round-bottomed flask equipped with a reflux condenser and is heated on a steam cone. Moderate nitrogen evolution commences immediately and continues for about 3 hours. When there are no more visible signs of gas evolution, the solution is cooled in an ice bath. After a few minutes, precipitation of light straw-colored clusters of prisms commences. About 6 g. of pure product, m.p. 70–72°, is obtained in this manner. Evaporation of the mother liquor yields another 4.5–5.5 g. of the oxide, slightly darker in color, m.p. 69–71°, which may be purified by recrystallization from 15 ml. of 70% ethanol to give material having a melting point of 70–71°. The total yield is 10.5–11.5 g. (80–85%).

2. Notes

1. If the *o*-nitroaniline is contaminated with *p*-nitroaniline, as it is likely to be, the yield and quality of the *o*-nitrophenylazide are lowered. The submitters obtained yields of 72–80% from *o*-nitroaniline melting at 70–71° obtained from the Eastman Kodak Company. The yields reported were obtained with *o*-nitroaniline melting at 72–73.5°.

2. A large container is necessary for this reaction because of excessive frothing which accompanies the nitrogen evolution. This step should be conducted in a hood to avoid possible exposure to hydrazoic acid.

3. A somewhat lower yield of benzofurazan oxide, m.p. 67–70°, is obtained if non-purified azide is used.

4. At this temperature there is no danger of decomposition. Loss of nitrogen commences at 80°.

5. Recrystallization of *o*-nitrophenylazide from a smaller volume of ethanol gives a considerably higher recovery, but it may be rather difficult to avoid separation of the product as an oil.

6. The submitters report that similar yields of phenylazide can be obtained from aniline in the same manner. Phenylazide must be distilled rather than recrystallized.²

3. Methods of Preparation

o-Nitrophenylazide has been prepared by the action of sodium azide or hydrazine on *o*-nitrobenzenediazonium sulfate;³ ammonia on *o*-nitrobenzenediazonium perbromide;^{4,5} *O*-benzylhydroxylamine hydrochloride on *o*-nitrobenzenediazonium acetate;⁶ sodium nitrite and hydrochloric acid on *o*-nitrophenylhydrazine;⁴ and aqueous alkali on *o*-nitrobenzenediazo- ψ -semicarbazino-camphor.⁷

Benzofurazan oxide has been prepared by a thermal decomposition of *o*-nitrophenylazide;^{4,8} by oxidation of the dioxime of *o*-benzoquinone by dilute nitric acid or potassium ferricyanide in alkaline solution;⁴ and by oxidation of *o*-nitroaniline with sodium hypochlorite.⁹ The present synthesis is a modification of the methods of Noelting and Kohn⁸ and of Zincke and Schwarz.⁴

¹ University of Michigan, Ann Arbor, Michigan.

² *Org. Syntheses*, **22**, 96 (1942).

³ Noelting and Michel, *Ber.*, **26**, 86, 88 (1893).

⁴ Zincke and Schwarz, *Ann.*, **307**, 28 (1899).

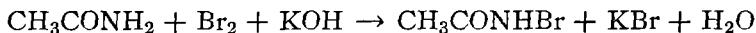
⁵ Noelting, Grandmougin, and Michel, *Ber.*, **25**, 3328 (1892).

⁶ Bamberger and Renault, *Ber.*, **30**, 2288 (1897).

⁷ Forster, *J. Chem. Soc.*, **89**, 233 (1906).

⁸ Noelting and Kohn, *Chem. Ztg.*, **18**, 1095 (1894).

⁹ Green and Rowe, *J. Chem. Soc.*, **101**, 2452 (1912).

N-BROMOACETAMIDE**(Acetamide, N-bromo-)**Submitted by EUGENE P. OLIVETO and CORINNE GEROLD.¹

Checked by RICHARD T. ARNOLD and CARL G. KRESPAN.

1. Procedure

Twenty grams of acetamide (0.34 mole) is dissolved in 54 g. of bromine (0.34 mole) contained in a 500-ml. Erlenmeyer flask, and the solution is cooled to 0-5° in an ice bath. An ice-cold aqueous 50% potassium hydroxide solution is added in small portions with swirling and cooling until the color becomes a light yellow. Approximately 33-34 ml. of the caustic solution is required. The nearly solid reaction mixture is allowed to stand at 0-5° for 2-3 hours.

The mixture is treated with 40 g. of salt and 200 ml. of chloroform and warmed on the steam bath with vigorous swirling. After 2-3 minutes the clear red chloroform layer is decanted from the semisolid lower layer, and the extraction is repeated twice more with 200- and 100-ml. portions of chloroform respectively (Note 1). The combined extracts are dried over sodium sulfate, the solution is filtered by gravity through a fluted filter into a 2-l. Erlenmeyer flask, and 500 ml. of hexane is added with swirling. White needles of N-bromoacetamide begin to form at once (Note 2). After chilling for 1-2 hours, the crystals are collected with suction, washed with hexane, and air-dried. The yield is 19-24 g. (41-51%), m.p. 102-105° (Note 3), purity 98-100% (Notes 4 and 5).

2. Notes

1. Six additional extractions, using 50-ml. portions of chloroform, may produce an increase in yield of 4-5 g.

2. Occasionally it may be necessary to add seed crystals to promote crystallization.

3. Material melting as much as 10° lower is sometimes obtained. However, it still has a purity of better than 96% as determined by thiosulfate titration (Note 4). This may indicate the presence of small amounts of N,N-dibromoacetamide.

4. The purity is determined by titration with standard sodium thiosulfate solution. An accurately weighed sample of about 200 mg. is dissolved in water, and a solution of approximately 1 g. of potassium iodide in 10 ml. of water is added. The solution is acidified with 10 ml. of 10% sulfuric acid and titrated with 0.1 *N* thiosulfate to the starch end point.

$$\% \text{ N-bromoacetamide} = \frac{\text{ml. S}_2\text{O}_3^{2-} \times \text{normality} \times 69 \times 100}{\text{weight of sample (mg.)}}$$

5. The product is unstable and should be stored in a cool place protected from light.

3. Methods of Preparation

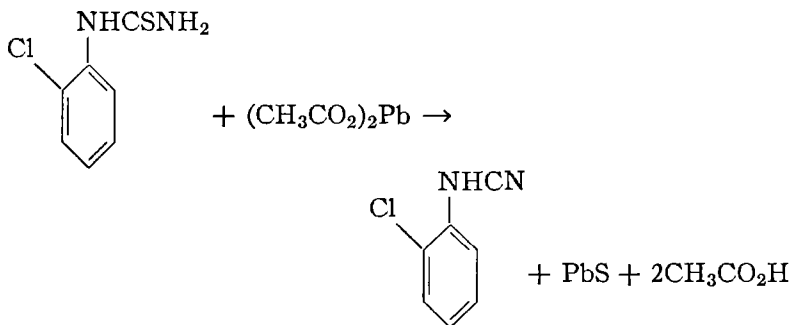
N-bromoacetamide has been prepared from acetamide and bromine in the presence of potassium hydroxide,^{2,3} zinc oxide,⁴ or calcium carbonate.⁴

¹ Schering Corporation, Bloomfield, New Jersey.

² Behrend and Schreiber, *Ann.*, **318**, 371 (1901).

³ Hofmann, *Ber.*, **15**, 407 (1882).

⁴ Likhoshesterov and Alekseev, *J. Gen. Chem. U.S.S.R.*, **3**, 927 (1933).

o-CHLOROPHENYLCYANAMIDE(Carbanilinonitrile, *o*-chloro-)Submitted by FREDERICK KURZER.¹

Checked by CLIFF S. HAMILTON and DAVID B. CAPPS.

1. Procedure

To a suspension of 37.4 g. (0.2 mole) of *o*-chlorophenylthiourea² in 300 ml. of water at 100°, contained in a 3-l. beaker, is added a boiling solution of 112 g. (2 moles) of potassium hydroxide in 300 ml. of water. The resulting solution is immediately treated with a hot saturated solution of 83.5 g. (0.22 mole) of lead acetate trihydrate, added as rapidly as possible and with good stirring (Note 1). The reaction mixture, from which large quantities of lead sulfide separate instantly, is boiled for 6 minutes and cooled to 0°, and the lead sulfide is filtered with suction by means of a large Büchner funnel (Note 2). The colorless filtrate is acidified at 0–5° (Note 3) by the slow addition with stirring of 120–140 ml. of glacial acetic acid. The white crystalline precipitate of nearly pure *o*-chlorophenylcyanamide which separates is collected by filtration on a suction filter and is washed with six 150-ml. portions of ice water. The crystalline mass of white plates is filtered, drained, and dried (Note 4). The yield of product, melting at 100–104°, is 26.28 g. (85–91%).

Recrystallization from benzene-light petroleum ether (8 ml. and 4 ml. respectively per gram of the dried precipitated material) gives lustrous needles of *o*-chlorophenylcyanamide, m.p. 105–106° (60–70% recovery) (Note 5). The above method is generally applicable and affords an excellent route to arylcyanamides (Note 6).

2. Notes

1. The exothermic reaction may cause the contents of the beaker to froth vigorously if the lead acetate solution is added too quickly. The reaction is readily controlled by adding the liquid in a rapid, thin stream with good stirring.

2. The use of a hardened filter paper or two thicknesses of ordinary filter paper is recommended. The black filter cake of lead sulfide may be extracted once again with 100 ml. of boiling 4% potassium hydroxide solution, and the extracts combined with the main filtrate.

3. The temperature of the solution is kept below 5° by the addition of suitable quantities of clean ice.

4. The product is sufficiently pure for use in further syntheses.

5. In benzene solution or in the solid state, *o*-chlorophenylcyanamide does not polymerize on storage for several months at 20–30°.

6. The desulfurization of arylthioureas can be used generally for preparing arylcyanamides in excellent yields. The submitter reports that α -naphthylcyanamide, melting at 124–128°, can be prepared in yields of 77–90% by this method.

3. Methods of Preparation

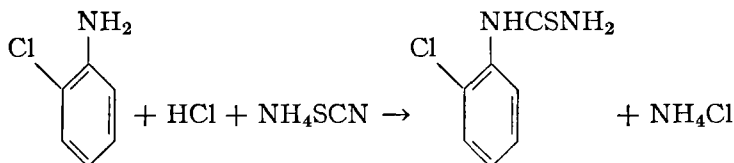
o-Chlorophenylcyanamide has been prepared by the action of lead acetate on *o*-chlorophenylthiourea.³ The method is based on the analogous preparation of phenylcyanamide.⁴

¹ University of London, London, England.

² *Org. Syntheses*, **31**, 21 (1951).

³ Kurzer, *J. Chem. Soc.*, **1949**, 3033.

⁴ Rathke, *Ber.*, **12**, 772 (1879); Krall et al., *J. Indian Chem. Soc.*, **10**, 343 (1942); **23**, 373 (1946).

o-CHLOROPHENYLTHIOUREA**[Urea, 1-(o-chlorophenyl)-2-thio-]**Submitted by FREDERICK KURZER.¹

Checked by CLIFF S. HAMILTON and DAVID B. CAPPS.

1. Procedure

To a suspension of 38.3 g. (31.5 ml., 0.30 mole) of *o*-chloroaniline in 300 ml. of warm water is added, with stirring, 27.5 ml. (0.33 mole) of concentrated hydrochloric acid (12 *N*). The resulting solution is placed in a 500-ml. porcelain evaporating dish, 25 g. (0.33 mole) of ammonium thiocyanate is added (Note 1), and the mixture is heated on the steam bath for 1 hour (Note 2). The liquid, from which a mass of large needles of *o*-chloroaniline thiocyanate separates, is allowed to cool, set aside at room temperature for 1 hour (Note 3), and then evaporated slowly to dryness over a period of 2–3 hours. The crystalline residue is crushed finely, 300 ml. of water is added, and again the mixture is evaporated slowly. The dry grayish white residual powder is heated finally on the steam bath for 4–5 hours.

The resulting mixture of crude *o*-chlorophenylthiourea and ammonium chloride (58–62 g.) is powdered finely and suspended in 300 ml. of water. The mixture is warmed slowly to 70° with mechanical stirring, then allowed to cool to 35°, and the solid is filtered with suction. The yield of crude *o*-chlorophenylthiourea, melting at 140–144°, is 30–35 g. (54–63%).

The crude material is dissolved in 60 ml. of absolute ethanol, the solution boiled with decolorizing carbon for a few minutes, and the clear, nearly colorless filtrate (Note 4) diluted with 100

ml. of hot benzene and 20 ml. of light petroleum ether (b.p. 60–80°). The white crystalline mass of *o*-chlorophenylthiourea, which separates gradually on cooling and standing, is separated by filtration under reduced pressure, washed with light petroleum ether, and dried, m.p. 144–146°. The yield of purified material is 20–24 g. (36–43%). Evaporation of the mother liquors and crystallization of the residue from a proportionally smaller volume of solvents yields a second crop (6–8 g.) (Note 5).

2. Notes

1. A good commercial grade of *o*-chloroaniline and pure ammonium thiocyanate are satisfactory for this preparation.

2. Comparable results are obtained when three times the quantities specified are used.

3. Uninterrupted evaporation of the initial reaction mixture sometimes tends to give a partly oily product from which only smaller yields can be obtained.

4. The filtration is best effected by the use of reduced pressure employing a preheated Büchner funnel and filter flask.

5. According to the submitter the method is generally applicable to the synthesis of aromatic thioureas. For example, phenylthiourea may be prepared in yields of 37–42%.

3. Methods of Preparation

o-Chlorophenylthiourea has been prepared from *o*-chlorophenylisothiocyanate and ammonia,² by the interaction of *o*-chloroaniline hydrochloride with sodium thiocyanate in chlorobenzene,³ or with ammonium thiocyanate in aqueous solution.⁴

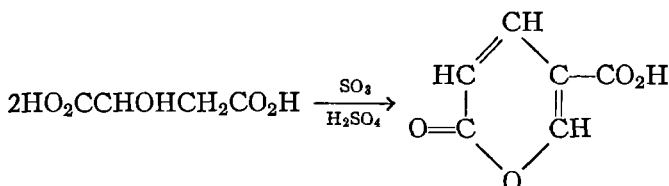
¹ University of London, London, England.

² Dyson and George, *J. Chem. Soc.*, **125**, 1705 (1924).

³ Dalglish and Mann, *J. Chem. Soc.*, **1945**, 900.

⁴ Kurzer, *J. Chem. Soc.*, **1949**, 3033.

COUMALIC ACID



Submitted by RICHARD H. WILEY and NEWTON R. SMITH.^{1,2}

Checked by C. F. H. ALLEN and GEORGE A. REYNOLDS.

1. Procedure

In a 2-l. round-bottomed flask are placed 200 g. (1.49 moles) of powdered malic acid (Note 1) and 170 ml. of concentrated sulfuric acid. To this suspension are added three 50-ml. portions of 20–30% fuming sulfuric acid at 45-minute intervals. After the evolution of gas has slackened, the solution is heated on a water bath for 2 hours with occasional shaking. The reaction mixture is then cooled and poured slowly onto 800 g. of crushed ice with stirring. After standing 24 hours, the acid is filtered on a Büchner funnel, washed with three 50-ml. portions of ice-cold water, and dried on a water bath. The yield of crude acid, melting at 195–200°, is 75–80 g. (Notes 2 and 3).

One-half of the crude product is dissolved in five times its weight of hot methanol, and the solution is boiled with 3 g. of Norit or decolorizing carbon. The solution is filtered while hot and cooled in an ice bath. The precipitate is collected on a filter and washed with 25 ml. of cold methanol. The mother liquors are used to recrystallize the remaining crude material. The yield of bright yellow coumalic acid, melting at 206–209°, is 68–73 g. (65–70%) (Note 4).

2. Notes

1. A technical free-flowing powder, melting at 126–128°, was used.

2. This washing is essential to remove the mineral acid and to avoid partial esterification that otherwise takes place during the methanol recrystallization step.

3. The submitters state that an additional 10-12 g. of crude acid can be obtained from the filtrate by extraction with ether in a continuous extractor.

4. Depending on the color of the crude acid, several additional recrystallizations may be required to obtain a colorless product.

3. Methods of Preparation

This procedure is essentially that of von Pechmann.³ Esters of coumalic acid may be obtained by heating the sulfuric acid solution with the appropriate alcohol.⁴

¹ University of Louisville, Louisville, Kentucky.

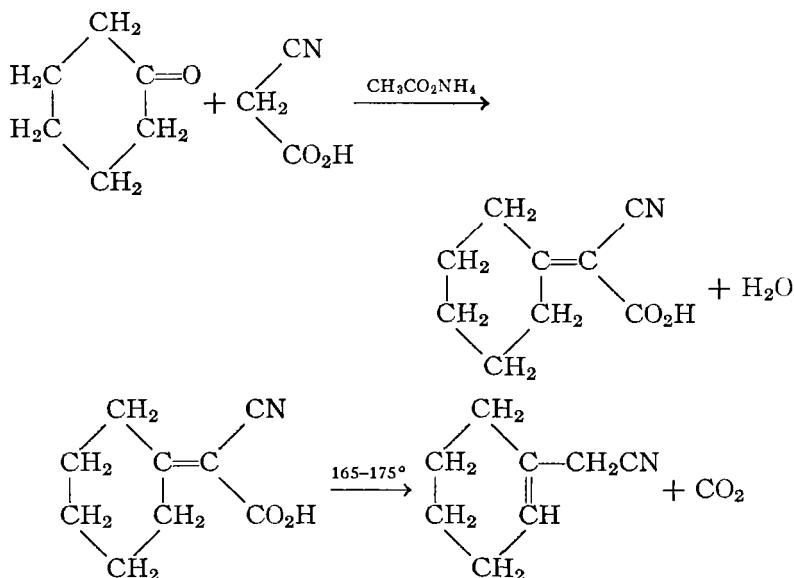
² The submitters wish to thank the Research Corporation for a grant under which this work was done.

³ von Pechmann, *Ann.*, **264**, 272 (1891).

⁴ Campbell and Hunt, *J. Chem. Soc.*, **1947**, 1176; Gilman and Burtner, *J. Am. Chem. Soc.*, **55**, 2903 (1933); Ruzicka, *Helv. Chim. Acta*, **4**, 504 (1921).

**CYCLOHEXYLIDENECYANOACETIC ACID AND
1-CYCLOHEXENYLACETONITRILE**

($\Delta^{1,\alpha}$ -Cyclohexanecetic acid, α -cyano-, and 1-Cyclohexene-1-acetonitrile)



Submitted by ARTHUR C. COPE, ALFRED A. D'ADDIECO,
DONALD EDWARD WHYTE, and SAMUEL A. GLICKMAN,¹
Checked by T. L. CAIRNS and R. E. HECKERT.

1. Procedure

In a 500-ml. round-bottomed flask equipped with a side arm through which a capillary tube is inserted (Note 1) are placed 108 g. (1.1 moles) of cyclohexanone (Note 2), 85 g. (1.0 mole) of cyanoacetic acid (Note 3), 3.0 g. (0.04 mole) of ammonium acetate (Note 4), and 75 ml. of benzene. The flask is attached to a modified Dean and Stark constant water separator,^{2,3} which in turn is attached to an efficient reflux condenser. The mixture is heated in an oil bath at $160-165^\circ$ so that a vigorous reflux

is maintained, and the water that collects in the separator is removed at intervals. The theoretical amount of water (18 ml.) is collected in the course of 2 hours, and the mixture is heated under reflux for an additional 1 hour. At this point, Part A is followed for the isolation of cyclohexylidenecyanoacetic acid, or Part B for the preparation of 1-cyclohexenylacetonitrile.

A. *Cyclohexylidenecyanoacetic acid*. The benzene solution is diluted with an additional 100 ml. of hot benzene and transferred to a 1-l. separatory funnel. The solution is allowed to cool until it is slightly above room temperature, and then 200 ml. of ether is added, small portions being used to rinse the reaction flask. After the solution has cooled to room temperature, it is washed with two 50-ml. portions of cold water (Note 5). The emulsion which normally forms at this point is broken by slow filtration through a Büchner funnel. The ether is removed, and the benzene solution is concentrated to approximately 300 ml. by distillation under reduced pressure. The solution is allowed to cool slowly to room temperature and then is cooled to about 10° in a refrigerator (Note 6). Cyclohexylidenecyanoacetic acid crystallizes as colorless prisms (Note 7). It is collected on a Büchner funnel, washed with two 100-ml. portions of cold benzene (10°), and dried in a vacuum desiccator to constant weight (88–92 g.). The filtrate and washings are concentrated by distillation under reduced pressure to about 150 ml. and cooled as in the first crystallization. The second crop of crystals is separated by filtration, washed with two 50-ml. portions of cold benzene (10°), and dried in a vacuum desiccator to constant weight (21–25 g.). Further concentration of the mother liquor and washings to a volume of about 75 ml. followed by cooling, filtering, washing with two 10-ml. portions of cold benzene, and drying yields an additional 2–5 g. The total yield of cyclohexylidenecyanoacetic acid, m.p. 110–110.5°, is 108–126 g. (65–76%).

B. *1-Cyclohexenylacetonitrile*. The benzene solution is allowed to cool to about 50°, and the flask is attached to a Vigreux column. The benzene is removed under reduced pressure, whereupon the residual cyclohexylidenecyanoacetic acid solidifies. The flask is then heated slowly in an oil bath to 165–175° while the system

is evacuated with a water pump to a pressure of 35–45 mm. (not lower). The acid melts, decarboxylation occurs very rapidly, and the crude 1-cyclohexenylacetonitrile distils at 100–120°/35–45 mm.

The crude product is diluted with 50 ml. of ether, washed with 10 ml. of 5% sodium carbonate solution then with 10 ml. of water, and dried over anhydrous sodium sulfate. The ether is removed by distillation, and the residue is distilled under reduced pressure. 1-Cyclohexenylacetonitrile is collected as a colorless liquid, b.p. 74–75°/4 mm. (110–112°/25 mm.), n_D^{25} 1.4769, in a yield of 92–110 g. (76–91%).

2. Notes

1. The capillary aids ebullition in the distillation under reduced pressure in Part B and may be omitted if cyclohexylidene-cyanoacetic acid is to be prepared according to Part A.

2. Commercial cyclohexanone obtained from the Barrett Division of the Allied Chemical and Dye Corporation was used.

3. Good quality commercial cyanoacetic acid was used. It may be purchased from the Benzol Products Company, Newark, New Jersey.

4. The amount of ammonium acetate specified permits completion of the condensation in a relatively short reaction period.

5. The product is washed with water to remove small amounts of ammonium acetate and acetamide which are formed from the ammonium acetate during the condensation.

6. If the rate of cooling is too fast at this point, very small crystals difficult to wash are formed. The rate and time of cooling also control the proportions of product found in the three fractions.

7. The solvated crystals effloresce upon drying, leaving a white solid which is easily powdered.

3. Methods of Preparation

Cyclohexylidenecyanoacetic acid has been prepared by the condensation of cyclohexanone and cyanoacetic acid in the presence of piperidine ^{4,5} and by the hydrolysis of ethyl cyclohexylidenecyanoacetate.⁴

1-Cyclohexenylacetone nitrile has been prepared by the decarboxylation of cyclohexylidenecyanoacetic acid;^{4,5} by the dehydration of 1-cyclohexenylacetamide;⁵ by the condensation of cyclohexanone and cyanoacetic acid in the presence of piperidine;⁶ by the condensation of cyclohexanone and ethyl cyanoacetate in the presence of sodium ethoxide;^{4,7} and by the condensation of cyclohexanone and cyanoacetic acid in the presence of ammonium acetate followed by decarboxylation.⁸ Ammonium acetate also has been used as a catalyst for the condensation of ketones with ethyl cyanoacetate.^{3,9}

In a number of instances the decarboxylation of α,β -unsaturated (conjugated) cyanoacetic acids has been found to yield β,γ -unsaturated (unconjugated) nitriles.^{5,10}

¹ Massachusetts Institute of Technology, Cambridge, Massachusetts.

² Dean and Stark, *Ind. Eng. Chem.*, **12**, 486 (1920).

³ Cope, Hofmann, Wyckoff, and Hardenbergh, *J. Am. Chem. Soc.*, **63**, 3452 (1941).

⁴ Harding, Haworth, and Perkin, *J. Chem. Soc.*, **93**, 1959 (1908).

⁵ Kandiah and Linstead, *J. Chem. Soc.*, **1929**, 2142, 2145.

⁶ Shemyakin and Trakhtenberg, *Compt. rend. acad. sci. U.R.S.S.*, **24**, 763 (1939) [*C. A.*, **34**, 3676 (1940)].

⁷ Birch and Kon, *J. Chem. Soc.*, **123**, 2444 (1923).

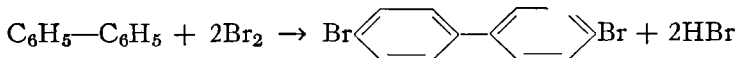
⁸ Whyte and Cope, *J. Am. Chem. Soc.*, **65**, 2002 (1943).

⁹ *Org. Syntheses*, **25**, 46 (1945).

¹⁰ von Auwers, *Ber.*, **56**, 1172 (1923).

4,4'-DIBROMOBIPHENYL

(Biphenyl, 4,4'-dibromo-)

Submitted by ROBERT E. BUCKLES and NORRIS G. WHEELER.¹Checked by R. S. SCHREIBER, WM. BRADLEY REID, JR., and
ROBERT W. JACKSON.

1. Procedure

In a 15-cm. evaporating dish is placed 15.4 g. (0.10 mole) of finely powdered biphenyl (Note 1). The dish is set on a porcelain rack in a 30-cm. desiccator with a 10-cm. evaporating dish under the rack containing 39 g. (12 ml., 0.24 mole) of bromine. The desiccator is closed, but a very small opening is provided for the escape of hydrogen bromide (Note 2). The biphenyl is left in contact with the bromine vapor for 8 hours (or overnight). The orange solid is then removed from the desiccator and allowed to stand in the air under a hood for at least 4 hours (Note 3). At this point, the product weighs about 30 g. and has a melting point in the neighborhood of 152°. The crude 4,4'-dibromobiphenyl is dissolved in 75 ml. of benzene, filtered, and cooled to 15°. The resulting crystals are filtered, giving a yield of 23.4–24.0 g. (75–77%) of 4,4'-dibromobiphenyl, m.p. 162–163° (Note 4).

2. Notes

1. The checkers used Eastman Kodak Company white label grade of biphenyl.
2. If a vacuum desiccator is used, the stopcock can be opened slightly to allow for the escape of hydrogen bromide.
3. The standing period allows hydrogen bromide and bromine to escape from the crystals.
4. 4,4'-Dibromobibenzyl can be prepared in the same manner. Eighteen grams (0.10 mole) of finely divided bibenzyl is left in

contact with the vapor from 39 g. (12 ml., 0.24 mole) of bromine for 24 hours. The desiccator is put under an opaque cover to keep out light, which causes the formation of α,α' -dibromobibenzyl. The somewhat sticky reaction product is allowed to stand overnight. The crude product is dissolved in 300 ml. of isopropyl alcohol, filtered, and cooled. A yield of 15.0-17.0 g. (44-50%) of 4,4'-dibromobibenzyl, m.p. 113-114°, is obtained.

3. Methods of Preparation

This method is a modification of that of Buckles, Hausman, and Wheeler.² 4,4'-Dibromobiphenyl has also been prepared by the bromination of biphenyl in water,³ carbon disulfide,⁴ and glacial acetic acid;⁵ by the bromination of a mixture of biphenyl-sulfonic acids in dilute sulfuric acid;⁶ by the action of sodium carbonate on the perbromide obtained from the reaction of diazotized benzidine with bromine water;⁷ and by passing *p*-dibromobenzene vapor through a red-hot tube.⁸

4,4'-Dibromobibenzyl has been prepared by the bromination of bibenzyl in water;⁹ by the reaction of *p*-bromobenzyl bromide with zinc dust in water;¹⁰ and by the reaction of bromobenzene with ethylene oxide in the presence of anhydrous aluminum chloride.¹¹

¹ The State University of Iowa, Iowa City, Iowa.

² Buckles, Hausman, and Wheeler, *J. Am. Chem. Soc.*, **72**, 2494 (1950).

³ Fittig, *Ann.*, **132**, 204 (1864).

⁴ Carnelley and Thompson, *J. Chem. Soc.*, **47**, 586 (1885).

⁵ Scholl and Neovius, *Ber.*, **44**, 1087 (1911).

⁶ Datta and Bhounik, *J. Am. Chem. Soc.*, **43**, 306 (1921).

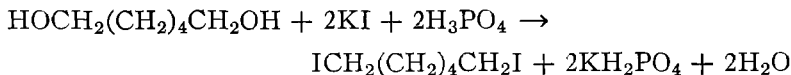
⁷ Griess, *J. Chem. Soc.*, **20**, 91 (1867).

⁸ Meyer and Hofmann, *Monatsh.*, **38**, 141 (1917).

⁹ Stelling and Fittig, *Ann.*, **137**, 267 (1866).

¹⁰ Errera, *Gazz. chim. ital.*, **18**, 236 (1888).

¹¹ Smith and Natelson, *J. Am. Chem. Soc.*, **53**, 3476 (1931).

1,6-DIIODOHEXANE**(Hexane, 1,6-diiodo-)**Submitted by HERMAN STONE and HAROLD SHECHTER.¹

Checked by T. L. CAIRNS, B. C. McKUSICK, and G. V. MOCK.

1. Procedure

In a 1-l. three-necked flask, equipped with a short reflux condenser, a sealed mechanical Hershberg stirrer, and a thermometer, is placed 65 g. (0.46 mole) of phosphoric anhydride, and 231 g. of 85% orthophosphoric acid (135 ml., 2 moles) is added (Note 1). After the stirred mixture has cooled to room temperature, 332 g. (2 moles) of potassium iodide and 59 g. (0.5 mole) of recrystallized 1,6-hexanediol (Notes 2, 3, and 4) are added. The mixture is stirred and heated at 100–120° for 3–5 hours, during which time the homogeneous solution separates into two phases, and finally a dense oil settles through the acid layer. The stirred mixture is cooled to room temperature, and 150 ml. of water and 250 ml. of ether are added (Note 5). The ether layer is separated, decolorized by shaking with 50 ml. of 10% sodium thiosulfate solution, washed with 200 ml. of cold saturated sodium chloride solution, and dried with 50 g. of anhydrous sodium sulfate. The ether is removed by distillation on a steam bath, and the product is distilled from a modified Claisen flask under reduced pressure. The fraction boiling at 123–128°/4 mm. is collected. The yield of 1,6-diiodohexane is 140–144 g. (83–85%), n_D^{15} 1.585, m.p. 10° (Notes 6 and 7).

2. Notes

1. The specified mixture of commercial 85% orthophosphoric acid and phosphoric anhydride corresponds to 95% orthophosphoric acid. Ninety-five per cent orthophosphoric acid is recom-

mended for this reaction. If 85% orthophosphoric acid is used, the reaction proceeds more slowly and the yield is reduced.

2. 1,6-Hexanediol,² m.p. 40–41°, was prepared by catalytic reduction of diethyl adipate with hydrogen over copper chromite catalyst. It can also be purchased from Columbia Organic Chemicals Company, Inc.

3. The solution must be cool before the potassium iodide is added to avoid the evolution of hydrogen iodide and formation of iodine. After the 1,6-hexanediol has been added, the mixture can be heated as desired since the hydrogen iodide reacts as rapidly as it is formed.

4. This procedure has been used successfully for conversion of various aliphatic and alicyclic alcohols to the corresponding iodides. Yields of iodides from 1-propanol, 2-methyl-1-propanol, 2-methyl-2-propanol, and cyclohexanol were 95, 88, 90, and 79.5%, respectively.

5. Usually one extraction of the reaction product with ether is sufficient to remove the color from the acid layer.

6. Slightly yellow 1,6-diiodohexane crystallizes as white needles when cooled in an ice-water mixture. The addition of a few drops of mercury to the yellow product produces a nearly colorless liquid.

7. The submitters reported yields of 93–95% and a melting point of 8.5–9.0°.

3. Methods of Preparation

1,6-Diiodohexane has been prepared in 73% yield by the reaction of 1,6-hexanediol, red phosphorus, and iodine.³ It has also been prepared by reactions of hydrogen iodide and 1,6-diphenoxyhexane⁴ and 1,6-diethoxyhexane,⁵ respectively. Physical constants have been reported by Dionneau.⁶

¹ Ohio State University, Columbus, Ohio.

² *Org. Syntheses* Coll. Vol. 2, 325 (1943).

³ Müller and Rölz, *Ber.*, **61**, 571 (1928).

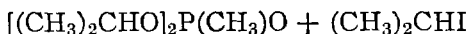
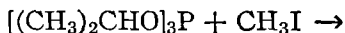
⁴ Salomina, *Ber.*, **26**, 2988 (1893).

⁵ Farmer, Laroia, Switz, and Thorpe, *J. Chem. Soc.*, **1927**, 2951.

⁶ Dionneau, *Ann. chim.*, [9] **3**, 257 (1915).

DIISOPROPYL METHYLPHOSPHONATE

(Methanephosphonic acid, diisopropyl ester)

Submitted by A. H. FORD-MOORE and B. J. PERRY.¹

Checked by WILLIAM S. JOHNSON and JAMES ACKERMAN.

1. Procedure

A 2-l. round-bottomed flask containing 284 g. (113 ml., 2 moles) of methyl iodide² is fitted with an efficient water-cooled condenser and a dropping funnel which is charged with 416 g. (453 ml., 2 moles) of triisopropyl phosphite (Note 1). A few pieces of porous plate are added to the methyl iodide, and about 50 ml. of the phosphite is introduced. The mixture is heated over a gauze with a free flame until an exothermic reaction begins. The flame is then withdrawn and the remainder of the phosphite is added at such a rate that the mixture keeps boiling briskly. Towards the end of the addition it may be necessary to reapply heat. After the addition is complete, the mixture is boiled under reflux for 1 hour. The condenser is replaced by a 50-75-cm. Vigreux column attached to a condenser set for distillation, and the bulk of the isopropyl iodide is distilled at 85-95° (atmospheric pressure). The residue is transferred to a pear-shaped flask for distillation through a 75-cm. Vigreux column under reduced pressure. The remainder of the isopropyl iodide is distilled at water-pump pressure, a Dry Ice trap being interposed between the receiver and the pump in order to effect complete condensation. A total of 310 g. (90%) of isopropyl iodide is thus recovered. The residue is then fractionated at vacuum-pump pressure. Except for a small fore-run and residue, the product distils almost entirely at 51°/1.0 mm. (46°/0.8 mm.). The yield of colorless product is 308-325 g. (85-90%); n_D^{20} 1.4101, n_D^{25} 1.4081; d_4^{24} 0.985, d_4^{10} 0.997 (Note 2).

2. Notes

1. The triisopropyl phosphite is prepared according to the procedure for triethyl phosphite³ and should be free from any diisopropyl hydrogen phosphite. The latter substance does not enter into the reaction but is difficult to remove from the final product. The starting material was supplied to the submitters by Messrs. Albright, Wilson and Company, Oldbury, Birmingham, England.

2. Diisopropyl ethylphosphonate can be obtained by a similar procedure, using the appropriate amount of ethyl iodide in place of methyl iodide. Ethyl iodide is less reactive, and it is necessary to apply heat during the addition of the phosphite and to allow the mixture to reflux for 7 hours after the addition. On a 2 *M* scale the yield is 354 g. (91%), b.p. 61°/0.7 mm., n_D^{25} 1.4108, d_4^{25} 0.968. The recovery of isopropyl iodide is 317 g. (93%).

Diethyl ethylphosphonate may be obtained by refluxing 332 g. (348 ml., 2 moles) of triethyl phosphite and 250 g. (1.6 moles) of ethyl iodide for 3 hours. After distillation of 231 g. (92%) of ethyl iodide, the residue is fractionated under reduced pressure, giving 329 g. (98.5%) of product, b.p. 56°/1 mm. (58.5°/1.8 mm.); n_D^{25} 1.4141, n_D^{20} 1.4161; d_4^{25} 1.022.

Diethyl methylphosphonate may be prepared similarly by refluxing one molar equivalent of triethyl phosphite with one mole of methyl iodide, but it is very difficult to separate the product from the small amount of diethyl ethylphosphonate that is formed simultaneously by the interaction of the phosphite with the ethyl iodide liberated in the reaction. The pure substance boils at 51°/1 mm., n_D^{25} 1.4117, d_4^{25} 1.050.

3. Methods of Preparation

The method described here for the preparation of diisopropyl methylphosphonate is a modification of the Arbusov rearrangement.⁴

¹ Chemical Defence Experimental Station, Porton, Nr. Salisbury, Wilts, England.

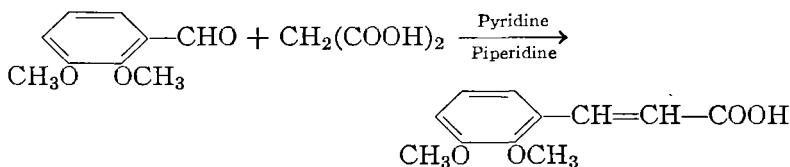
² *Org. Syntheses* Coll. Vol. 2, 404 (1943).

³ *Org. Syntheses*, 31, 111 (1951).

⁴ Arbusov, *Chem. Centr.*, [II] 77, 1640 (1906); Ford-Moore and Williams, *J. Chem. Soc.*, 1947, 1465.

2,3-DIMETHOXYCINNAMIC ACID

(Cinnamic acid, 2,3-dimethoxy-)



Submitted by J. KOO, M. S. FISH, G. N. WALKER, and J. BLAKE.¹

Checked by T. L. CAIRNS and A. E. BARKDOLL.

1. Procedure

In a 3-l. round-bottomed flask (Note 1), fitted with a reflux condenser and a thermometer, are placed 208 g. (2 moles) of malonic acid (Note 2), 166 g. (1 mole) of 2,3-dimethoxybenzaldehyde (Note 3), and 400 ml. of pyridine. The malonic acid is dissolved by shaking and warming on a steam bath (Note 4). Piperidine (15 ml.) is then added, the reflux condenser and thermometer are fitted into place (Note 5), and the mixture is heated to 80°. About 30 minutes should be allowed for this rise in temperature. An internal temperature of 80–85° is maintained for 1 hour, and the material is finally heated under reflux (109–115°) for an additional 3 hours (Note 6).

After being cooled the reaction mixture is poured into a large beaker containing 4 l. of cold water. The mixture is acidified by slowly adding with stirring 500 ml. of concentrated hydrochloric acid; it should be strongly acidic at this point. The light-brown crystals are separated by suction filtration and washed 4 times with 150-ml. portions of cold water. The crude

acid is dissolved in a solution of 80 g. of sodium hydroxide in 3 l. of water. The resulting solution is filtered, diluted with an additional 1.2 l. of water, and acidified by adding with stirring 600 ml. of 1:1 hydrochloric acid. The mixture is filtered, and the crystalline material is washed with three 150-ml. portions of cold water. The product is dried at 60–70° (Note 7). The yield is 180–205 g. (87–98%), m.p. 174–178° (Note 8). Further purification is usually not necessary, but it may be accomplished by recrystallization from methyl ethyl ketone, using 12 ml. of solvent per gram of acid. The hot solution is filtered rapidly through a steam-heated Büchner funnel and chilled for several hours. A recovery of 70% of product, m.p. 179–180°, may be obtained.

2. Notes

1. A large flask is preferred to insure against possible loss by foaming.

2. An excess of malonic acid is necessary for high yields. An equimolecular amount of malonic acid results in yields as low as 50%.

3. A practical grade of 2,3-dimethoxybenzaldehyde gives satisfactory results. It is convenient to weigh and transfer this material as a liquid.

4. If the malonic acid is not in solution before addition of the piperidine, the reaction cannot be controlled properly. It is advisable to heat the mixture to 50° to effect solution.

5. The thermometer may be suspended in the mixture through the condenser by means of a long wire.

6. Evolution of carbon dioxide begins at about 55–60°. The prescribed temperatures are necessary to prevent undue foaming.

7. The product should be dried to constant weight in an oven. Drying for several days is usually required.

8. This method is a general one. It can be used with a variety of substituted aromatic aldehydes.

3. Methods of Preparation

2,3-Dimethoxycinnamic acid has been prepared by heating 2,3-dimethoxybenzaldehyde with acetic anhydride and sodium acetate at 200°² and by the condensation of 2,3-dimethoxybenzaldehyde and ethyl acetate with sodium, followed by hydrolysis.³ The present preparation represents an adaption of the Doebner reaction.

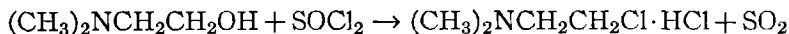
¹ University of Pennsylvania, Philadelphia, Pennsylvania.

² von Krannichfeldt, *Ber.*, **46**, 4021 (1913).

³ Perkin and Robinson, *J. Chem. Soc.*, **105**, 2387 (1914).

β -DIMETHYLAMINOETHYL CHLORIDE HYDROCHLORIDE

(Ethylamine, 2-chloro-N,N-dimethyl-, hydrochloride)



Submitted by LUTHER A. R. HALL, VERLIN C. STEPHENS, and
J. H. BURCKHALTER.¹

Checked by RICHARD T. ARNOLD and WILLIAM LEE.

1. Procedure

Caution! This preparation should be conducted in a good hood.

In a dry 1-l. flask fitted with a sealed mechanical stirrer, an efficient reflux condenser, and a 500-ml. dropping funnel is placed 290 g. (2.44 moles) of thionyl chloride (Note 1). The reaction flask must be cooled in an ice bath throughout the entire period of operation, as the reaction is very exothermic. β -Dimethylaminoethanol (210 g., 2.35 moles) (Note 2) is added dropwise through the funnel to the cooled thionyl chloride (Note 3) over a period of an hour, during which time there is a copious evolution of sulfur dioxide (Note 4). After all the β -dimethylaminoethanol has been added, the ice bath is removed and the reaction mixture is stirred for another hour (Note 5). The temperature of the mixture is 35–50°. At this point the reaction mixture

consists of a brown semisolid slush of the desired product together with a slight excess of thionyl chloride.

The entire contents of the reaction flask are transferred to a 2-l. beaker (or wide-mouthed Erlenmeyer flask) containing approximately 1 l. of absolute ethanol (Note 6). The resulting brown solution is heated to boiling on a hot plate, during which time there is a copious evolution of gases (Note 6). The solution is filtered hot, leaving a small amount of insoluble material. Upon cooling of the filtrate in a salt-ice bath, the desired product is obtained as beautiful white crystals which are collected on a Büchner funnel and dried in a vacuum desiccator over phosphorus pentoxide (Note 7). The yield of pure product melting at 201.5–203° is 227–272 g. (67–80%).

Upon evaporation of the last filtrate to one-third of its volume and cooling in a salt-ice bath, an additional 33–69 g. (10–20%) of good-quality product is obtained. The total yield is 296–305 g. (87–90%).

2. Notes

1. Eastman Kodak Company practical grade thionyl chloride is satisfactory.

2. A good commercial grade (Eastman Kodak Company or Union Carbide and Carbon Corporation) of β -dimethylaminoethanol is satisfactory.

3. Continued and efficient cooling of the reaction vessel is needed to prevent too vigorous an evolution of sulfur dioxide and a subsequent loss of thionyl chloride through trapping of this reagent by effluent gases. Cooling also prevents too high a reaction temperature. The reaction proceeds more smoothly if the temperature is kept below 50°.

4. Care should be taken that the dropping funnel inlet does not become clogged with solid product. If the tip of the dropping funnel is in such a position that the drops of β -dimethylaminoethanol fall directly into the thionyl chloride and do not drain down the walls of the flask, mechanical difficulties are reduced markedly. The reaction must be carried out in an efficient hood or with a suitable trap in order to remove the noxious sulfur dioxide formed.

5. The reaction mixture may be stirred for a longer time and allowed to stand overnight without affecting the yield.

6. The ethanol not only converts the excess thionyl chloride to gaseous by-products (sulfur dioxide, hydrogen chloride, and ethyl chloride) but also serves as the recrystallizing solvent for the desired product. The checkers found that about 80% of this thick product can be poured directly into 800 ml. of ethanol. Two hundred milliliters of warm ethanol should be used to decompose the product remaining in the reaction flask. This is combined with the main portion.

7. The product is somewhat hygroscopic, especially in humid weather. It should be dried in a vacuum desiccator to prevent the formation of hydrated forms.

3. Methods of Preparation

β -Dialkylaminoethyl bromide hydrobromides have been known for many years. However, the standard method of preparation requires large volumes of hydrobromic acid.² The less expensive analogous chlorides are preferred since their preparation is simpler and their reactivity is sufficient for the synthesis of well-known drugs.³ Ordinarily β -dialkylaminoalkyl chloride hydrochlorides are prepared in good yield by treatment of β -dialkylaminoalkanols with an excess of thionyl chloride in chloroform or benzene.⁴ An article on the German commercial preparation of Atabrine refers to the action of thionyl chloride on β -diethylaminoethanol hydrochloride without solvent.⁵

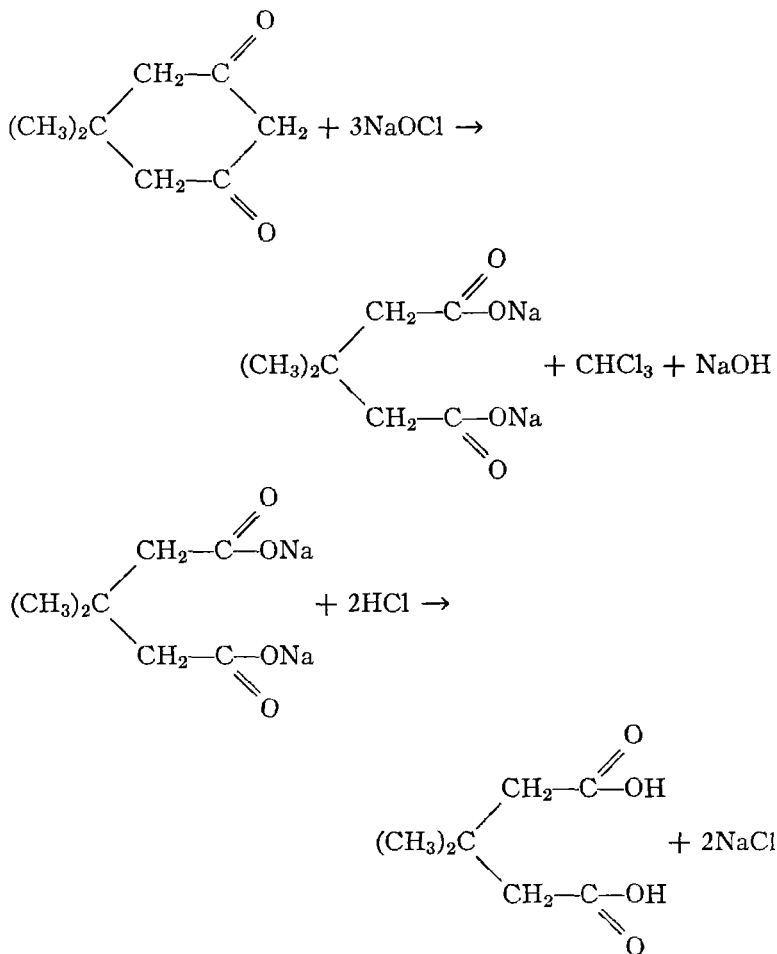
¹ University of Kansas, Lawrence, Kansas.

² *Org. Syntheses* Coll. Vol. 2, 92 (1943).

³ Hutter et al., *J. Am. Chem. Soc.*, **68**, 1999 (1946).

⁴ Burger, *J. Am. Pharm. Assoc., Sci. Ed.*, **36**, 372 (1947); Tchoubar and Letellier-Dupré, *Bull. soc. chim. France*, **1947**, 792; Elderfield et al., *J. Am. Chem. Soc.*, **68**, 1579 (1946); Marechal and Bagot, *Ann. pharm. franc.*, **4**, 172 (1946); Giral and Cascajares, *Ciencia (Mex.)*, **5**, 105 (1944) [*C. A.*, **41**, 4892 (1947)]; Ward, U. S. pat. 2,072,348 [*C. A.*, **31**, 2614 (1937)]; Mannich and Baumgarten, *Ber.*, **70**, 210 (1937); Brit. pat. 456,338 [*C. A.*, **31**, 2230 (1937)]; French pat. 802,416 [*C. A.*, **31**, 1824 (1937)]; Slotta and Behnisch, *Ber.*, **68**, 754 (1935); Gough and King, *J. Chem. Soc.*, **1928**, 2436; Meister, Lucius, and Brünig, Brit. pat. 167,781 [*Brit. Abstracts*, **122**, 529 (1922)].

⁵ Greene, *Am. J. Pharm.*, **120**, 39 (1948).

β,β -DIMETHYLGLUTARIC ACID(Glutaric acid, β,β -dimethyl-)

Submitted by WALTER T. SMITH and GERALD L. McLEOD.¹
 Checked by WILLIAM S. JOHNSON and DONALD D. CAMERON.

1. Procedure

A solution of 218 g. (5.45 moles) of sodium hydroxide in 300 ml. of water in a 3-l. three-necked flask is cooled to room temperature. To this solution 1250 g. of ice is added, and a stream of chlorine is passed in rapidly through a delivery tube having a small opening and extending almost to the bottom of the liquid. The passage of the chlorine is continued until 161 g. (2.27 moles) has been absorbed. The flask is then fitted with a mechanical stirrer, a thermometer, and a 500-ml. separatory funnel.

Seventy grams (0.5 mole) of methone² is dissolved in a solution of 65 g. (1.16 moles) of potassium hydroxide in 525 ml. of water. The solution is cooled to room temperature, poured into the separatory funnel, and run slowly with stirring into the sodium hypochlorite solution. The temperature rises gradually to 35–40° during the addition. After the addition has been completed, the solution is stirred for 6–8 hours until the temperature drops to room temperature.

Without interrupting the stirring, 50 g. of sodium sulfite is added to decompose the excess sodium hypochlorite, and the solution is acidified to Congo red by adding concentrated hydrochloric acid slowly with stirring to avoid foaming. The acid solution is then concentrated by distillation until salts just begin to precipitate (Note 1).

The mixture is then cooled to room temperature, 300 ml. of ether and enough water are added to dissolve all of the precipitate, and the whole is transferred to a 3-l. separatory funnel. The layers are separated, and the aqueous portion is extracted with three 200-ml. portions of ether. The ether extracts are combined and dried for several hours over 15–20 g. of anhydrous magnesium sulfate. The ether is then removed by distillation. This may be conveniently carried out by fitting a 250-ml. Claisen flask with a separatory funnel in order to add the solution as the ether distills. When only 150–200 ml. of solution remains in the flask, the distillation is stopped and the residue is poured into a small beaker. The remaining ether is removed by heating on a steam bath, and the residue solidifies on cooling. The

colorless, crystalline β,β -dimethylglutaric acid is dried in air. The yield is 73-77 g. (91-96%), m.p. 97-99°. Crystallization from 100-125 ml. of benzene gives 65-73 g. (81-91%) of acid, m.p. 100-102° (Note 2).

2. Notes

1. The chloroform formed in the reaction comes over during the early stages of this distillation. The precipitation of salts usually begins after the solution has been concentrated to about one-half the original volume.

2. The melting points given in the literature are 101°,³ 101-102°,⁴ 103-104°,⁵ and 98-100°.⁶

3. Methods of Preparation

β,β -Dimethylglutaric acid has been prepared by heating dimethylpropanetricarboxylic acid above its melting point;³ by hydrolysis of the condensation product of ethyl cyanoacetate and ethyl β,β -dimethylacrylate;⁷ by the action of sulfuric acid on diethyl β,β -dimethyl- α,α' -dicyanoglutarate;⁸ by hydrolysis of the nitrile obtained by the action of calcium cyanide on β,β -dimethylbutyrolactone;⁴ by the action of sulfuric acid on β,β -dimethyl- α,α' -dicyanoglutarimide;⁹ and by the action of sodium hypobromite on methone.⁵ The present procedure is essentially that of Walker and Wood.⁶

¹ The State University of Iowa, Iowa City, Iowa.

² *Org. Syntheses* Coll. Vol. 2, 200 (1943).

³ Perkin and Goodwin, *J. Chem. Soc.*, **69**, 1472 (1896).

⁴ Blaise, *Compt. rend.*, **126**, 1153 (1898).

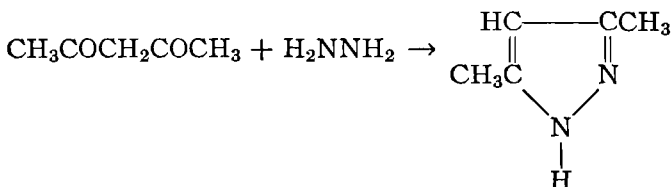
⁵ Guareschi, *Atti reale accad. sci. Torino*, [1] **36**, 261 (1900-1901) [*Chem. Centr.*, [1] **72**, 821 (1901)].

⁶ Walker and Wood, *J. Chem. Soc.*, **89**, 598 (1906).

⁷ Perkin and Thorpe, *J. Chem. Soc.*, **75**, 48 (1899).

⁸ Komppa, *Ber.*, **33**, 3531 (1900).

⁹ Komppa, *Ber.*, **32**, 1423 (1899).

3,5-DIMETHYLPYRAZOLE**(Pyrazole, 3,5-dimethyl-)**

Submitted by RICHARD H. WILEY and PETER E. HEXNER.¹
 Checked by WILLIAM S. JOHNSON and ROBERT J. HIGHT.

1. Procedure

Sixty-five grams (0.50 mole) of hydrazine sulfate (Note 1) is dissolved in 400 ml. of 10% sodium hydroxide in a 1-l. round-bottomed flask, fitted with a separatory funnel, a thermometer, and a stirrer. The flask is immersed in an ice bath and cooled. When the temperature of the mixture reaches 15° (Note 2), 50 g. (0.50 mole) of acetylacetone (Note 3) is added dropwise with stirring while the temperature is maintained at about 15°. The addition requires about 30 minutes to complete, and the mixture is stirred for 1 hour at 15° (Note 4). The contents of the flask are diluted with 200 ml. of water to dissolve precipitated inorganic salts, transferred to a 1-l. separatory funnel, and shaken with 125 ml. of ether. The layers are separated, and the aqueous layer is extracted with four 40-ml. portions of ether. The ether extracts are combined, washed once with saturated sodium chloride solution, and dried over anhydrous potassium carbonate. The ether is removed by distillation, and the slightly yellow residue of crystalline 3,5-dimethylpyrazole obtained by drying at reduced pressure (approximately 20 mm.) weighs 37–39 g. (77–81%), m.p. 107–108°. This product, which is of good quality, can be recrystallized from about 250 ml. of 90–100° petroleum ether without significant change in appearance or melting point.

The yield after drying in a vacuum desiccator containing paraffin chips is 35–37 g. (73–77%) (Note 5).

2. Notes

1. Hydrazine sulfate supplied by the Eastman Kodak Company is satisfactory, or it may be prepared by a previously described procedure.²

2. A precipitate of sodium sulfate may form at this point.

3. Union Carbide and Carbon Corporation technical 2,4-pentanedione was used without purification.

4. The 3,5-dimethylpyrazole precipitates during this period.

5. Recrystallization from methanol or ethanol gives practically colorless material of the same melting point, but it is more difficult to obtain good recovery owing to the high solubility of the pyrazole in these solvents.

3. Methods of Preparation

3,5-Dimethylpyrazole has been prepared from acetylacetone and hydrazine hydrate in ethanol³ or hydrazine sulfate in aqueous alkali.^{4,5,6} The latter method is preferred, because the reaction with hydrazine hydrate is sometimes violent.^{3,4} 3,5-Dimethylpyrazole has also been prepared by hydrolysis and decarboxylation of the 1-carbamido- or 1-carboxamidine derivatives, obtained by reaction of semicarbazide⁷ or aminoguanidine⁸ with acetylacetone.

¹ University of Louisville, Louisville, Kentucky.

² *Org. Syntheses* Coll. Vol. 1, 309 (1941).

³ Rothenberg, *J. prakt. Chem.*, [2] 52, 50 (1895); *Ber.*, 27, 1097 (1894).

⁴ Rosengarten, *Ann.*, 279, 237 (1894).

⁵ Morgan and Ackerman, *J. Chem. Soc.*, 123, 1308 (1923).

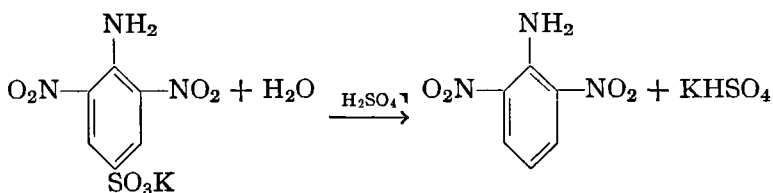
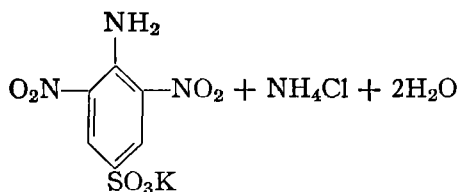
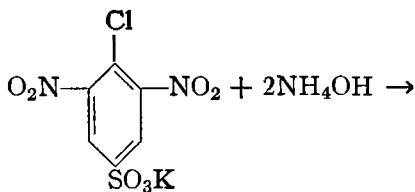
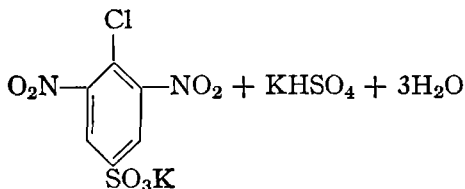
⁶ Zimmerman and Lochte, *J. Am. Chem. Soc.*, 60, 2456 (1938).

⁷ Posner, *Ber.*, 34, 3980 (1901).

⁸ Thiele and Dralle, *Ann.*, 302, 294 (1898).

2,6-DINITROANILINE

(Aniline, 2,6-dinitro-)

Submitted by HARRY P. SCHULTZ.¹

Checked by ARTHUR C. COPE and DOUGLAS S. SMITH.

1. Procedure

In a 1-l. round-bottomed flask fitted with a mechanical stirrer are placed 50 ml. (55.4 g., 0.49 mole) of chlorobenzene (Note 1), 300 ml. of concentrated sulfuric acid (sp. gr., 1.84), and 50 ml. (92 g.) of fuming sulfuric acid (containing approximately 25%

free sulfur trioxide). The mixture is stirred and heated on a steam bath for 2 hours and then cooled to room temperature. The stirrer is removed from the reaction flask and replaced with a thermometer. To the clear solution is added 170 g. (1.68 moles) of potassium nitrate in 4 portions. The temperature of the mixture during this time is held at 40–60° by cooling the flask and its contents in ice water. After the mixture has been swirled briefly in the reaction flask to dissolve most of the potassium nitrate, it is heated to 110–115° (Note 2) and held at that temperature for 20 hours. The hot contents of the flask are poured onto 2 kg. of cracked ice. After the ice has melted, the yellow precipitate is filtered with suction and pressed as dry as possible.

Without further drying, the potassium 4-chloro-3,5-dinitrobenzenesulfonate is recrystallized from 600 ml. of boiling water (Note 3). Insoluble material is removed by decantation and filtration of the hot solution. The solution is cooled to 5–10° for 12 hours, and the crystalline potassium salt is collected on a suction filter, pressed as dry as possible, and placed at once in a solution of 400 ml. of concentrated ammonium hydroxide (sp. gr. 0.90) in 400 ml. of water. The solution is boiled for 1 hour under a reflux condenser which has been connected to a gas absorption trap,² and then is cooled at 5–10° for 12 hours. The orange, crystalline potassium 4-amino-3,5-dinitrobenzenesulfonate is filtered with suction and pressed as dry as possible on a 10-cm. Büchner funnel.

The damp salt is placed in a solution of 200 ml. of concentrated sulfuric acid (sp. gr. 1.84) and 200 ml. of water in a 1-l. round-bottomed flask, and the mixture is boiled vigorously under reflux for 6 hours (Note 4). The hot acid solution is poured onto 1 kg. of cracked ice, filtered on a 7.5-cm. Büchner funnel, slurried twice with 100-ml. portions of water, and pressed as dry as possible on the funnel. The damp, impure 2,6-dinitroaniline is dissolved in 500 ml. of hot 95% ethanol, and the solution is boiled under reflux for 10 minutes with 3 g. of Norit and 3 g. of filter aid. The hot ethanol solution is filtered through a heated funnel (Note 5) and cooled slowly to room temperature. Light-orange

needles of 2,6-dinitroaniline separate and are collected on a suction filter and air-dried. The yield is 27.4–32.3 g. (30–36%) (Note 6), m.p. 139–140°.

2. Notes

1. The best grade of Eastman Kodak Company chlorobenzene was used.

2. Since the reaction is moderately exothermic during the first 4 hours, the temperature of the reaction mixture must be controlled carefully. A gas trap² may be used to absorb the small amount of nitrogen dioxide evolved, or the reaction may be carried out in a hood. Excessive fuming is avoided if the temperature is kept in the range 110–115°.

3. If the potassium 4-chloro-3,5-dinitrobenzenesulfonate is not recrystallized before ammonolysis very impure 2,6-dinitroaniline is obtained.

4. The condenser should be cleared occasionally with a small glass rod to remove the 2,6-dinitroaniline that may collect there.

5. The funnel must be heated to avoid crystallization during filtration.

6. The solubility of pure 2,6-dinitroaniline in 95% ethanol at room temperature is about 0.4 g. per 100 ml.

3. Methods of Preparation

2,6-Dinitroaniline has been prepared by the ammonolysis of 2,6-dinitroanisole,³ 2,6-dinitroiodobenzene,⁴ 2,6-dinitrophenyl 4-nitrobenzyl ether,⁵ and 2,6-dinitrochlorobenzene;⁶ by the rearrangement of *o*-nitrophenylnitramine;⁷ and by the desulfonation of potassium 4-amino-3,5-dinitrobenzenesulfonate.^{8,9} The method described above is based upon the procedures of Ullmann⁸ and Welsh.⁹

¹ University of Miami, Coral Gables, Florida.

² *Org. Syntheses* Coll. Vol. 2, 4 (1943).

³ Salkowski, *Ann.*, **174**, 273 (1874).

⁴ Koerner, *Gazz. chim. ital.*, **4**, 324 (1874).

⁵ Kumpf, *Ann.*, **224**, 118 (1884).

⁶ Borsche and Rantscheff, *Ann.*, **379**, 162 (1911).

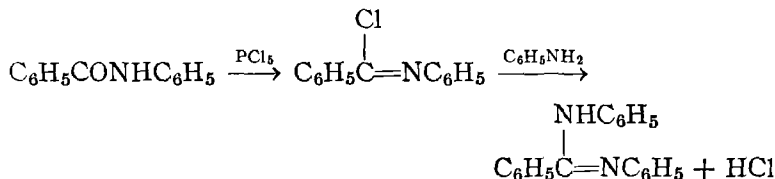
⁷ Hoff, *Ann.*, **311**, 108 (1900).

⁸ Ullmann, Engi, et al., *Ann.*, **366**, 102 (1909).

⁹ Welsh, *J. Am. Chem. Soc.*, **63**, 3276 (1941).

N,N'-DIPHENYLBENZAMIDINE

(Benzamidine, N,N'-diphenyl-)



Submitted by ARTHUR C. HONTZ and E. C. WAGNER.¹

Checked by R. S. SCHREIBER and WM. BRADLEY REID, JR.

1. Procedure

In a 1-l. three-necked round-bottomed flask (Note 1) are placed 90.0 g. (0.456 mole) of benzanilide ² (Note 2) previously dried in an oven at 120° (Note 3) and 95 g. (0.456 mole) (Note 4) of phosphorus pentachloride. The solids are mixed by shaking, and lumps are reduced by manipulation with a rod. A short reflux condenser and a small dropping funnel are attached.

The mixture is heated in an electric mantle or oil bath at 110° for 30 minutes and heated under reflux at 160° for 90 minutes or until active evolution of hydrogen chloride ceases (Note 5). To the mixture are added slowly through a dropping funnel first 36.4 g. (0.46 mole) of pyridine (Note 6) previously dried over pellet-form potassium hydroxide, and then 42.4 g. (0.456 mole) of freshly distilled aniline. The contents of the flask are mixed

by swirling. The mixture is heated at 160° for about 20 minutes or until the red color is discharged, at which point the flask is removed from the source of heat. The mixture is cooled to about 90°, and 250 ml. of water is added slowly through the dropping funnel with agitation to ensure separation of the solid product in granular form. After the mixture has cooled to room temperature, the solid is collected on a Büchner funnel and air-dried.

The crude diphenylbenzamidinium hydrochloride is transferred to a 1-l. beaker and treated with 500 ml. of 28% ammonia water (hood). The mixture is stirred mechanically and warmed very gently for an hour. The diphenylbenzamidinium is collected on a Büchner funnel and air-dried. The melting point of the product at this stage is 130–136°.

To purify the product it is recrystallized from 80% ethanol (Note 7), using 8–10 ml. per gram of diphenylbenzamidinium. The small insoluble residue of unconverted hydrochloride which may remain (Note 8) is removed by filtering the hot solution. The solution is chilled in an ice-salt bath, and the crystalline product is collected on a Büchner funnel, pressed dry, and finally dried in the air or in an oven at 100°. The yield is 91–100 g. (73–80%) (Note 9) of product having a melting point of 142–144° (Notes 10 and 11). Recrystallization of 100 g. of this material from 800 ml. of 80% ethanol gives 87 g. (87% recovery) of pure N,N'-diphenylbenzamidinium, m.p. 144–145°.

2. Notes

1. An all-glass apparatus is desirable as cork connections are attacked during formation of the imidochloride. The checkers used mechanical stirring.

2. The benzanilide should be of good quality, or tarry material will form and interfere with purification of the product. Benzanilide is readily made by the Schotten-Baumann procedure from aniline, 10% aqueous sodium hydroxide, and benzoyl chloride in the proportions 6:30:5, and after crystallization from 95% ethanol is sufficiently pure.

3. The use of benzanilide dried by fusion ³ did not improve the yield.

4. The use of one-fourth an equivalent of phosphorus pentachloride, in an attempt to utilize fully the dehydroxylating capacity of both phosphorus pentachloride and the derived phosphorus oxychloride, led to a low yield of diphenylbenzamidine (50%) and to formation of tarry material that interfered with purification. By use of phosphorus oxychloride ⁴ instead of the pentachloride, a temperature of 170° was required to keep the mixture liquid, tarry material was considerable, and the operation was generally unsatisfactory.

5. Isolation of the imidochloride by distillation under reduced pressure offers no advantage.

6. Pyridine serves to make all the aniline available. It does not prevent combination of hydrogen chloride with the N,N'-diphenylbenzamidine even when two equivalents of pyridine are used. In the presence of pyridine the reaction mixture is a suspension and is easily handled. In the absence of pyridine it solidifies to a cake, which must be pulverized to permit liberation of the amidine from the hydrochloride.

7. A series of tests showed ethanol of 78–82% by weight (sp. gr. 0.8344–0.8442 at 25.5°; 84–87% by volume) to be the best solvent. To dissolve 1.0 g. of N,N'-diphenylbenzamidine at the boiling point required 15.5 ml. of 94% (by weight) ethanol, 7.24 ml. of 80% ethanol, and 11 ml. of 71% ethanol, and the recoveries on chilling were respectively 45%, 73%, and 45%; ten intermediate concentrations of ethanol gave results consistent with these. The solubility of N,N'-diphenylbenzamidine in methanol is greater than in ethanol, but recovery is relatively low.

8. The undissolved residue is unchanged hydrochloride and is usually small. If considerable it may be re-treated with ammonia and the free base recovered.

9. By chilling to 20° the yield is about 68% of pure material that melts at 144–145°. A second crop of less pure material can be obtained from the mother liquor by concentrating and chilling. By chilling in a Dry Ice-ethanol bath the yield is about 80% but the product is less pure. Admixed tarry material may be re-

moved in large part by extraction with cold ether, in which the tar dissolves readily.

10. The checkers used a Fisher-Johns block.

11. This method is capable of extension to the preparation of other N,N'-disubstituted amidines.⁵ In some preparations it may be advantageous to remove phosphorus oxychloride by distillation under reduced pressure before addition of the amine. The method is not wholly satisfactory for preparation of N,N'-diarylformamidines, which are better made by the orthoformic ester method.⁶ During preparation of diphenylacetamide considerable gluey material formed by decomposition of the intermediate N-phenylacetimidochloride⁷ is an impediment to the isolation of the product.⁸ This amidine is better prepared by the method of Sen and Ray.⁹

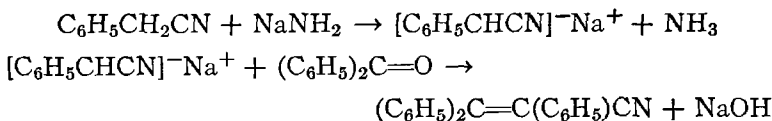
3. Methods of Preparation

N,N'-Diphenylbenzamidines and closely related amidines have been made by several procedures which involve interaction of amines with N-substituted imidochlorides either preformed¹⁰ or formed *in situ* from an acylamine by action of phosphorus trichloride,¹¹ phosphorus oxychloride,⁴ or phosphorus pentachloride.⁵ Diphenylbenzamidines are formed from aniline and benzanilidochloroiodide,¹² from aniline and phenylbenzimidio ether,¹³ and from aniline hydrochloride and N-phenylbenzamidines.¹⁴ It is obtained also from carbanilide and benzoyl chloride,¹⁵ from carbodiphenylimide and phenylmagnesium bromide,¹⁶ and from aniline hydrochloride and benzonitrile at 220–240°.¹⁷ Amidines, including diphenylbenzamidines, are obtainable from nitriles by heating with ammonium or amine salts of sulfonic acids,¹⁸ by heating benzotrichloride with amines,¹⁹ and from Schiff bases by action of *tert.*-amyl hypochlorite.²⁰ Good yields are claimed for a patented process using an acylamine, benzenesulfonyl chloride, and amine in the presence of pyridine.²¹ The method described is based upon the procedures of Wallach³ and Hill and Cox.⁵

- ¹ University of Pennsylvania, Philadelphia, Pennsylvania.
- ² *Org. Syntheses* Coll. Vol. 1, 82 (1941).
- ³ Wallach, *Ann.*, **184**, 79 (1877); Holljes and Wagner, *J. Org. Chem.*, **9**, 43 (1944).
- ⁴ Sidiki and Shah, *J. Univ. Bombay*, **6**, II, 132 (1937).
- ⁵ Hill and Cox, *J. Am. Chem. Soc.*, **48**, 3214 (1926).
- ⁶ von Walther, *J. prakt. Chem.*, **53**, 473 (1896).
- ⁷ von Braun, Jostes, and Heymons, *Ber.*, **60**, 93 (1927).
- ⁸ W. F. Tomlinson, University of Pennsylvania, 1947, unpublished results.
- ⁹ Sen and Rây, *J. Chem. Soc.*, **1926**, 646.
- ¹⁰ Gerhardt, *Ann.*, **108**, 219 (1858).
- ¹¹ Hofmann, *Z. Chem.*, **1866**, 165.
- ¹² Lander and Laws, *J. Chem. Soc.*, **85**, 1696 (1904).
- ¹³ Lossen and Kobbelt, *Ann.*, **265**, 155 (1891).
- ¹⁴ Bernthsen, *Ann.*, **184**, 355 (1877).
- ¹⁵ Dains, *J. Am. Chem. Soc.*, **22**, 190 (1900).
- ¹⁶ Busch and Hobein, *Ber.*, **40**, 4297 (1907).
- ¹⁷ Bernthsen, *Ann.*, **184**, 349 (1877).
- ¹⁸ Oxley and Short, *J. Chem. Soc.*, **1946**, 147; U. S. pat. 2,433,489 [*C. A.*, **42**, 3780 (1948)].
- ¹⁹ Joshi, Khanolkar, and Wheeler, *J. Chem. Soc.*, **1936**, 793.
- ²⁰ Fusco and Musante, *Gazz. chim. ital.*, **66**, 258 (1936).
- ²¹ *Brit. pat.* 577,478 [*C. A.*, **42**, 7321 (1948)].

α,β -DIPHENYLCINNAMONITRILE

(Acrylonitrile, triphenyl-)



Submitted by STANLEY WAWZONEK and EDWIN M. SMOLIN.¹

Checked by ARTHUR C. COPE and MALCOLM CHAMBERLAIN.

1. Procedure

Caution! This preparation should be conducted in a hood to avoid exposure to ammonia.

A solution of sodium amide in liquid ammonia is prepared according to a procedure previously described (Note 1) in a 2-l. three-necked round-bottomed flask fitted with a reflux condenser

attached to a soda-lime tower which is connected to a gas absorption trap,² a mercury-sealed mechanical stirrer, and an inlet tube. Anhydrous liquid ammonia (350 ml.) is introduced through the inlet tube, and about 0.3 g. of hydrated ferric nitrate and 13.7 g. (0.59 gram atom) of freshly cut sodium are added (Notes 1 and 2).

After the conversion of sodium to sodium amide is complete, the inlet tube is replaced with a 500-ml. dropping funnel and the flask is cooled in a bath of Dry Ice and trichloroethylene. Benzyl cyanide (69 g., 0.59 mole) (Note 3) is added dropwise with stirring during about 20 minutes. The cooling bath is removed, and the solution is stirred for an additional period of 20 minutes, after which 700 ml. of dry ether is added slowly through the dropping funnel. The solution is allowed to stand or is warmed gently with a water bath until it comes to room temperature. The rate of addition of ether and subsequent warming are controlled so that the ammonia which is vaporized passes through the gas absorption trap rather than escaping in part through the mercury seal of the stirrer. When most of the ammonia has been removed, an additional 300-ml. portion of dry ether is added (Note 4). The flask is then heated on a hot water bath. By turning off the cooling water of the reflux condenser for a short time, a small amount of ether is allowed to distil out of the reaction mixture in order to remove as much of the ammonia as possible (Note 5). The condenser water is then turned on again, and dry nitrogen lines under a positive pressure of 2-3 cm. of mercury (maintained by a T-tube dipping into mercury) are attached to the top of the dropping funnel and the reflux condenser. A solution of 200 g. (1.1 moles) of benzophenone (Notes 6 and 7) in 300 ml. of dry ether (Note 8) is added through the dropping funnel during a period of 15 minutes, and the mixture is heated under reflux with stirring for 24 hours. At the end of this period the solution contains a reddish brown precipitate. The mixture is allowed to cool, and 250 ml. of water is added slowly through the dropping funnel. The aqueous and ether layers are separated in a 2-l. separatory funnel, and the water layer is filtered directly through a 15-cm. Büchner funnel. The aqueous

filtrate is discarded. The ether layer also is run into the funnel, and the filtrate is concentrated to a volume of about 80 ml. The solid that separates is added to the solid previously collected on the filter. The crude reddish brown product is recrystallized from 600 ml. of glacial acetic acid. α,β -Diphenylcinnamonnitrile separates as white crystals which are collected on a suction filter, washed with 100 ml. of water, and dried at 110° for 24 hours. The yield of a pure product melting at $166\text{--}167^\circ$ is 83–110 g. (50–66%).

2. Notes

1. The procedures for preparing sodium amide and the sodium derivative of benzyl cyanide are described in *Organic Syntheses*.³ Another procedure for preparing sodium amide⁴ is convenient and should be equally satisfactory.

2. If vaporization of ammonia reduces the liquid volume to less than 250 ml. before the conversion of sodium to sodium amide is complete, more ammonia should be added through the inlet tube.

3. The benzyl cyanide used should be washed with warm 50% sulfuric acid to remove benzyl isocyanide⁵ and redistilled.

4. Some of the ether is lost through the reflux condenser during vaporization of the ammonia.

5. Traces of ammonia remain in the reaction mixture after this procedure.

6. A smaller excess of benzophenone results in a lowered yield.

7. The benzophenone should be dried by redistillation or storage over phosphorus pentoxide in a vacuum desiccator.

8. The mixture of benzophenone and ether should be warmed gently until the solid dissolves.

3. Methods of Preparation

α,β -Diphenylcinnamonnitrile has been prepared by the condensation of benzophenone with the sodium derivative of benzyl cyanide,⁶ or from benzophenone, benzyl cyanide, and sodium

ethoxide.⁷ It has been obtained by heating benzyl cyanide with benzophenone dichloride at 200°.⁸

¹ The State University of Iowa, Iowa City, Iowa.

² *Org. Syntheses* Coll. Vol. 2, 4 (1943).

³ *Org. Syntheses*, 25, 25 (1945).

⁴ *Org. Syntheses*, 30, 72 (1950).

⁵ *Org. Syntheses* Coll. Vol. 1, 108 (1941).

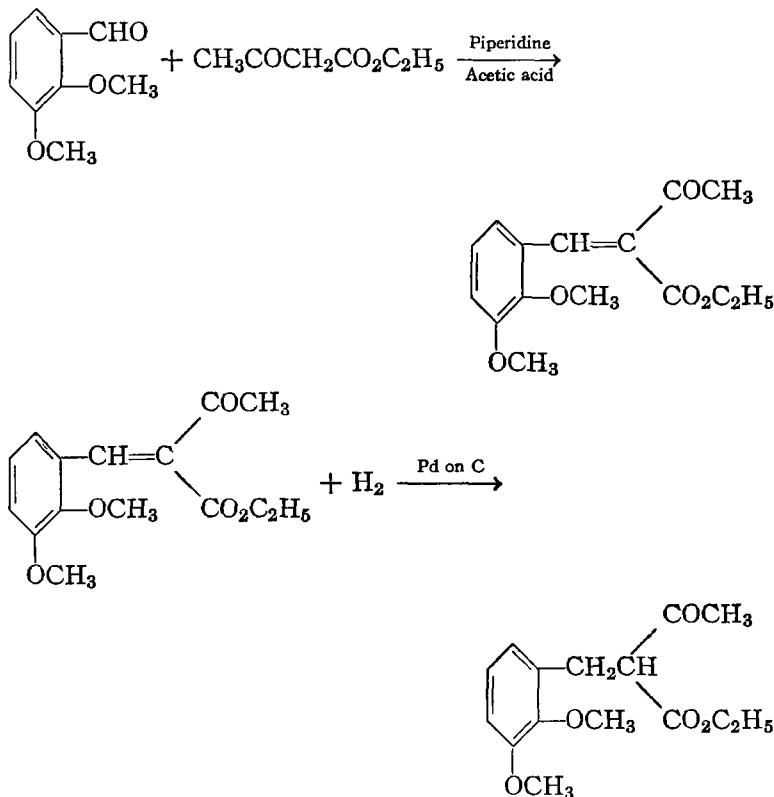
⁶ Bodroux, *Bull. soc. chim. France*, [4] 9, 758 (1911).

⁷ Stobbe and Zeitschel, *Ber.*, 34, 1967 (1901).

⁸ Heyl and Meyer, *Ber.*, 28, 1798, 2785 (1895).

**ETHYL α -ACETYL- β -(2,3-DIMETHOXYPHENYL)-
PROPIONATE**

(Hydrocinnamic acid, α -acetyl-2,3-dimethoxy-, ethyl ester)



Submitted by E. C. HORNING, J. KOO, M. S. FISH, and G. N. WALKER.¹
 Checked by T. L. CAIRNS and CHARLES W. TODD.

1. Procedure

A. Ethyl α -acetyl- β -(2,3-dimethoxyphenyl)acrylate. In a 1-l. round-bottomed flask fitted with a water-benzene separator² and a reflux condenser are placed 183 g. (1.1 moles) of 2,3-dimethoxy-

oxybenzaldehyde (Note 1) and 130 g. (1.0 mole) of ethyl acetoacetate. The water-benzene separator is filled with benzene, an additional 70 ml. of benzene is added to the mixture, and the 2,3-dimethoxybenzaldehyde is brought into solution by warming. Piperidine (4 ml.) and glacial acetic acid (12 ml.) are added, and the mixture is heated under reflux for 2–3 hours (Note 2). The mixture is cooled, poured into a separatory funnel with 800 ml. of ether, and washed successively with 200-ml. portions of 5% hydrochloric acid, 5% sodium bicarbonate solution, and 5% acetic acid, and twice with water. The extract is dried over anhydrous magnesium sulfate (about 250 g.). After filtration, the ether and benzene are distilled under atmospheric pressure, and the residue is distilled under reduced pressure. The yield of viscous, yellow oil collected at 186–190°/2 mm. (Note 3) is 180–199 g. (64–72%), n_D^{25} 1.5507–1.5508.

B. *Ethyl α -acetyl- β -(2,3-dimethoxyphenyl)propionate.* The product obtained in Part A is divided into two approximately equal portions, and to each are added 125 ml. of ethyl acetate and 5 g. of 5% palladium-on-carbon catalyst (Note 4). Each solution is shaken with hydrogen at pressures between 20 and 40 lb. in a low-pressure apparatus. About 45 minutes is usually needed for complete reduction. The two solutions are then combined, and the catalyst is removed by filtration and washed with 20 ml. of ethyl acetate. The ethyl acetate is distilled at atmospheric pressure, and distillation of the residue under reduced pressure yields 158–176 g. (56–63% over-all) of a colorless product collected at 175–177°/3 mm., n_D^{25} 1.5042–1.5044 (Notes 3 and 5).

2. Notes

1. A practical grade of 2,3-dimethoxybenzaldehyde, although discolored, is satisfactory. It is best handled and weighed as a liquid. This is done by warming the container on a steam bath for several minutes.

2. The time of reflux is determined by the rate at which water separates from the reaction mixture. In general, the theoretical amount of water (18 ml.) is collected in the water separator after

about 1 hour, but additional refluxing usually results in the separation of another 4-5 ml. Anhydrous materials are not necessary for the reaction.

3. Using a 6-in. Vigreux column with a wide side arm, the checkers observed a boiling point of 166-168°/3 mm. for ethyl α -acetyl- β -(2,3-dimethoxyphenyl)propionate and 176-179°/2 mm. for the acrylate.

4. These quantities are convenient for hydrogenation in a Parr low-pressure apparatus; if a larger apparatus is available, it is unnecessary to divide the material. The palladium-on-carbon catalyst is prepared by Hartung's method,³ using sufficient Norit to give a 5% catalyst. A few chips of Dry Ice should be placed in the bottle before the catalyst is added to provide an inert atmosphere. The checkers used a catalyst obtained from Baker and Company, Inc., 113 Astor Street, Newark, New Jersey.

5. The same procedure may be used with other aromatic aldehydes. The acrylate ester prepared from veratraldehyde is a crystalline compound melting at 82.5-84.5°. It may be purified by distillation under reduced pressure, b.p. 190-196°/0.8 mm. The yield is 53-63%. The hydrogenated product is obtained as a colorless oil, b.p. 180-183°/1.0 mm., in 38-44% over-all yield.

3. Methods of Preparation

Substituted α -benzylacetoacetic esters have usually been prepared by the general method of Leuchs,⁴ in which ethyl acetoacetate is alkylated in ethanol solution with benzyl chloride and sodium ethoxide. The present method is based upon Cope's⁵ procedure for the condensation of carbonyl compounds with ethyl acetoacetate, followed by catalytic reduction of the condensation product.

¹ University of Pennsylvania, Philadelphia, Pennsylvania.

² *Org. Syntheses*, **23**, 38 (1943).

³ *Org. Syntheses*, **26**, 77 (1946), Method D.

⁴ Leuchs, *Ber.*, **44**, 1510 (1911).

⁵ Cope and Hofmann, *J. Am. Chem. Soc.*, **63**, 3456 (1941).

ETHYL PYRUVATE
(Pyruvic acid, ethyl ester)



Submitted by J. W. CORNFORTH.¹

Checked by CHARLES C. PRICE, KENNETH N. CAMPBELL, and JOHN WARNE.

1. Procedure

In a 1-l. round-bottomed flask, fitted with a thermometer and a mechanical stirrer, are placed 130 ml. of saturated aqueous magnesium sulfate solution, 500 ml. of light petroleum ether (Note 1), 50 g. (0.42 mole) of ethyl lactate (Note 2), and 20 g. (0.13 mole) of sodium dihydrogen phosphate dihydrate. The stirrer is started (Note 3), the temperature is brought to 15° by means of an ice-water bath, and 55 g. (0.35 mole) of powdered potassium permanganate is added during 25–30 minutes. Stirring is continued until the oxidation is complete (Note 4), the temperature being kept near 15° throughout the process. The petroleum ether solution is decanted and the sludge stirred with three 50-ml. portions of light petroleum ether. The combined petroleum ether extracts are evaporated on a steam bath under a short fractionating column (Note 5). The residual oil is shaken thoroughly with two 10-ml. portions of a saturated aqueous calcium chloride solution (Note 6) and then distilled under reduced pressure. Almost the whole product boils at 56–57°/20 mm. The yield is 25–27 g. (51–54%) of nearly pure ethyl pyruvate, n_D^{20} 1.4053. This product compares favorably with material prepared by esterification of pyruvic acid (Note 7). Further purification may be effected through the sodium bisulfite compound (Note 8).

2. Notes

1. Petroleum ether, b.p. 40–60°, was washed with concentrated sulfuric acid before use. The checkers used the hexane fraction of petroleum.

2. The ethyl lactate should be of good quality, as its impurities tend to appear in the final product. The submitter used a good commercial grade supplied by British Industrial Solvents, Ltd. Its specification included an ester content of not less than 99% (calculated as ethyl lactate).

The commercial 99% ethyl lactate available to the checkers did not give satisfactory results. It was purified by distillation through a fractionating column 8 by $\frac{3}{4}$ in., packed with glass beads. The portion having the following properties was used: b.p. 154–155°, n_D^{20} 1.4125, d_4^{20} 1.0302.

3. The thick lower layer is stirred continuously and not too fast. Vigorous agitation of the upper layer is not advisable. A short Hershberg wire stirrer was used.

4. The oxidation requires about 2.5 hours. Unreduced permanganate is easily detected by spotting on filter paper. If a cake of manganese dioxide is formed beyond the compass of the stirrer, it should be pushed down. It is rarely necessary to do this more than once.

5. The distillate of petroleum ether, which contains ethanol and some ethyl pyruvate, can be recovered for another run by shaking with a little concentrated sulfuric acid.

6. This treatment removes unoxidized ethyl lactate. Each shaking should be continued for 5 minutes. It is convenient to separate the layers by centrifuging. Droplets of calcium chloride solution should not be present in the oil when it is to be distilled, or some polymerization will occur.

7. No satisfactory criterion of purity for ethyl pyruvate is available in the literature. The submitter used a method of assay which was devised² for the estimation of aldehydes. One hundred and sixteen milligrams of the ester is weighed in a 100-ml. conical flask, dissolved in 5 ml. of water, and treated with 0.3 ml. of saturated sodium bisulfite solution. After 1–2 minutes,

a little starch solution is added, the mixture is chilled, and 0.1 *N* iodine solution is run in as rapidly as possible until the blue color is stable for a few seconds (about 12 ml. is required). Six milliliters of saturated sodium bicarbonate solution is added, and titration with iodine solution is carried out in the ordinary way. The end point is stable for 1 minute or more. The theoretical volume of 0.1 *N* iodine required for pure ethyl pyruvate in the second stage is 20 ml. Thus if *n* ml. is required the estimated purity is $5n\%$. The results are perfectly consistent but may be slightly lower than the true values owing to dissociation of the bisulfite complex. The results from four different samples are as tabulated.

METHOD OF PREPARATION	ESTIMATED ETHYL PYRUVATE CONTENT (%)
(1) Oxidation of ethyl lactate	95
(2) Esterification of once-distilled pyruvic acid	93-94
(3) Sample (2) twice redistilled; fraction b.p. 147-148° taken	96
(4) Sample (1) purified through bisulfite complex (Note 8)	98.5

8. The bisulfite compound is best made in small batches. The ester (2.2 ml.) in a large test tube is underlaid with 3.6 ml. of saturated sodium bisulfite solution. The tube is chilled in a freezing mixture, and the layers are shaken together. Crystallization occurs rapidly, especially if seed crystals are present. After 3 minutes, 10 ml. of ethanol is added and the crystalline product is washed on a filter with ethanol and ether. The yield is 3.0 g. Sixteen grams of the bisulfite complex is mixed with 32 ml. of saturated magnesium sulfate solution, and 5 ml. of 40% formaldehyde is added. After shaking, the oil is separated and the aqueous layer extracted with a little ether, which is added to the oil. After drying with magnesium sulfate the product is distilled at low pressure and affords 5.5 g. of ethyl pyruvate, b.p. 56°/20 mm. On redistillation, the purified ester boils at 147.5°/750 mm., n_D^{20} 1.4052, f.p. around -50°.

3. Methods of Preparation

Ethyl pyruvate can be prepared by esterification of pyruvic acid^{3,4} or by catalytic oxidation of ethyl lactate with air or oxygen.^{5,6} A process has been patented for the oxidation of ethyl lactate by acidified permanganate in dilute aqueous solution.⁷ Of minor interest are the preparations by pyrolysis of ethyl α -triphenylmethoxypropionate⁸ and by the action of diethylamine on ethyl *meso*- α,α' -dibromoadipate.⁹

¹ National Institute for Medical Research, London, England.

² Clausen, *J. Biol. Chem.*, **52**, 263 (1922).

³ Archer and Pratt, *J. Am. Chem. Soc.*, **66**, 1656 (1944).

⁴ Simon, *Bull. soc. chim. France*, [3] **13**, 474 (1895).

⁵ C. H. Boehringer Sohn, Ger. pat. 447,838 [*Frdl.*, **15**, 382 (1928)].

⁶ Kulka, *Can. J. Research*, **24B**, 221 (1946).

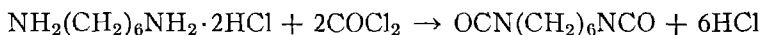
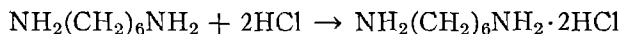
⁷ Byk-Guldenwerke Chem. Fab. A. G., Ger. pat. 526,366 [*C. A.*, **25**, 4285 (1931)].

⁸ Hurd and Filachione, *J. Am. Chem. Soc.*, **59**, 1949 (1937).

⁹ von Braun, Leistner, and Münch, *Ber.*, **59**, 1953 (1926).

HEXAMETHYLENE DIISOCYANATE

(Isocyanic acid, hexamethylene ester; **1**, **6**-Hexanediol, diisocyanate)



Submitted by MARK W. FARLOW.¹

Checked by R. L. SHRINER and ROBERT C. JOHNSON.

1. Procedure

Caution! Hexamethylenediamine, hexamethylene diisocyanate, and phosgene are highly toxic. Exposure to vapors or solutions containing these materials should be avoided. All operations should be conducted in a hood.

A. Hexamethylenediammonium chloride. To a solution of 116 g. (1.0 mole) of hexamethylenediamine (Note 1) in 145 ml. of methanol in a 1-l. beaker is added slowly from a dropping funnel, 175 ml. of concentrated hydrochloric acid (sp. gr. 1.19).

The mixture is well stirred during the addition and cooled externally to keep the contents below 30°. The hexamethylenediammonium chloride is then precipitated by adding the solution slowly with stirring to approximately 2 l. of acetone. The precipitate is collected on a Büchner funnel, washed with 100 ml. of cold acetone, and dried in a vacuum oven at 75° for 12–18 hours (Note 2). The yield of dry product amounts to 170–187 g. (90–99%), m.p. 243–246° (Note 3).

B. *Hexamethylene diisocyanate*. A suspension of 94.5 g. (0.50 mole) of finely powdered hexamethylenediammonium chloride in 500 ml. of anhydrous redistilled amylbenzene (or tetralin) (Note 4) is prepared in a 1-l. three-necked flask fitted with an efficient mechanical stirrer (Note 5), a water-cooled reflux condenser, a thermometer, and a phosgene inlet tube (Note 6) extending well below the surface of the suspension. Stirring is started, the mixture is heated to 180–185° (Note 7), and gaseous chlorine-free phosgene (Note 8) is delivered to the mixture at a rate of about 33 g. (0.33 mole) per hour. Hydrogen chloride and excess phosgene escape through the condenser. The temperature is carefully maintained between 180° and 185°; after 8–15 hours (Note 9) solution of the hexamethylenediammonium chloride is essentially complete and hydrogen chloride is no longer evolved (Note 10). The reaction mixture is then filtered through a suction filter, and the filtrate is distilled at reduced pressure through a fractionating column, giving amylbenzene, b.p. 65–75°/10 mm. (Note 11), and 70–80 g. (84–95%) of hexamethylene diisocyanate boiling at 120–125°/10 mm. (92–96°/1 mm., 108–111°/5 mm.); n_D^{20} 1.4585; d_4^{20} 1.0528 (Note 12).

2. Notes

1. Hexamethylenediamine may be obtained from the Polychemicals Department, E. I. du Pont de Nemours and Company, Inc., Wilmington, Delaware. Usually the commercial product is a 70% aqueous solution from which the water may be distilled at atmospheric pressure. The residue is suitable for preparing the dihydrochloride.

2. Thorough drying of the hydrochloride is essential to the success of the next step. Overnight drying in a vacuum oven at 70–100° is effective. The dry salt is not appreciably hygroscopic, but it should be preserved in a well-stoppered bottle until used.

3. This salt shows a marked tendency to sublime at and above 200°.

4. Commercial amylbenzene is dried by distillation, and the fraction boiling at 184–194° is collected. This solvent has been withdrawn from the market (1950), and hence tetralin may be substituted. Commercial tetralin is washed with ferrous sulfate solution and distilled; the fraction boiling at 202–206° is used. *o*-Dichlorobenzene has also been recommended as a solvent.²

5. Efficient agitation of the gas-liquid-solid reaction mixture is conducive to a high rate of reaction. The use of a reaction flask modified with creases³ has given good results.

6. The end of the inlet tube should have a very coarse fritted glass disk in order to promote rapid reaction. A tube with a bulb in which many fine holes have been blown may also be used, but the reaction time is longer. If the inlet tube becomes clogged, it may be cleaned quickly by removing it from the reaction flask and dipping in warm cresol, which dissolves any polyhexamethylene urea that may form. The tube is then rinsed with amylbenzene or tetralin and replaced in the reaction flask.

7. The temperature of the reaction mixture should be maintained between 180° and 185° in order to obtain as rapid a reaction as possible. Higher temperatures lead to the formation of polyhexamethylene urea. A run carried out at the boiling point of tetralin (206°) gave an 84% yield of polymer.

8. Phosgene is available from the Niagara Chlorine Products Co., Inc., Lockport, New York, or the Matheson Co., Inc., Rutherford, New Jersey. When phosgene containing small amounts of chlorine is used, the reaction appears to proceed normally but the product and recovered solvent are contaminated with chlorine-containing impurities. Chlorine in phosgene can be detected by bubbling a stream of the gas rapidly through

clean mercury. Chlorine reacts with and discolors the mercury, whereas pure phosgene leaves the mercury unchanged. If chlorine is present, it may be removed by bubbling the phosgene through two wash bottles containing cottonseed oil.

9. The time required for complete reaction is dependent on the reaction temperature, on the design of the phosgene inlet tube, on the efficiency of agitation, and on the rate of phosgene addition. It is important that the reaction be continued until practically all the hexamethylenediammonium chloride has disappeared. If unreacted amine salt is present, it has a tendency to sublime with the diisocyanate during distillation.

10. When moist air is blown through a glass tube held at the end of the condenser, across the current of phosgene containing hydrogen chloride, the fogging typical of hydrogen chloride gas in a moist atmosphere is produced. Pure phosgene gives no visible effect under similar conditions.

11. The recovered solvent is suitable for succeeding preparations. If tetralin is used as the reaction medium, it is recovered as the low-boiling fraction, b.p. 60–70°/8 mm.

12. If the product contains chlorine as indicated by the alcoholic silver nitrate test, it may be purified by adding a small amount of anhydrous calcium oxide (0.5 g. per 50 g. of product) and redistilling under reduced pressure.

3. Methods of Preparation

Hexamethylene diisocyanate has been prepared by the action of phosgene on hexamethylenediammonium chloride ⁴ or on hexamethylenediammonium carbonate.⁵ Metal chlorides such as those of cobalt, iron, mercury, or zinc have been stated to promote the reaction.²

¹ E. I. du Pont de Nemours and Company, Inc., Wilmington, Delaware.

² Burgoine and New, Imperial Chemical Industries, Ltd., Brit. pat. 574,222 [C. A., **42**, 7788 (1948)].

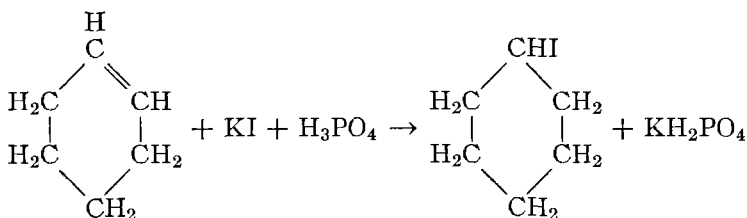
³ Morton, Darling, and Davidson, *Ind. Eng. Chem., Anal. Ed.*, **14**, 734 (1942).

⁴ Farlow, E. I. du Pont de Nemours and Company, Inc., U. S. pat. 2,374,340 [C. A., **39**, 3555 (1945)].

⁵ Smith, P. B. 7416, *Synthetic Fiber Developments in Germany*, p. 47, Textile Research Institute, Inc., New York, New York, 1946.

IODOCYCLOHEXANE

(Cyclohexane, iodo-)



Submitted by HERMAN STONE and HAROLD SHECHTER.¹

Checked by T. L. CAIRNS and V. A. ENGELHARDT.

1. Procedure

Forty-one grams (0.5 mole) of cyclohexene (Note 1) is added to a mixture of 250 g. (1.5 moles) of potassium iodide in 221 g. (2.14 moles) of 95% orthophosphoric acid (Notes 2, 3, and 4) contained in a 1-l. three-necked flask equipped with a reflux condenser, a sealed mechanical stirrer, and a thermometer. The mixture is stirred and heated at 80° for 3 hours, after which it is allowed to cool and treated with 150 ml. of water and 250 ml. of diethyl ether with continued stirring (Notes 5 and 6). The ether extract is separated, decolorized with 50 ml. of 10% aqueous sodium thiosulfate solution, washed with 50 ml. of saturated sodium chloride solution, and dried with anhydrous sodium sulfate (50 g.). The ether is evaporated on a steam bath, and the product is distilled from a modified Claisen flask under reduced pressure. The portion boiling at 48–49.5°/4 mm. is collected. The yield of iodocyclohexane is 93–95 g. (88–90%), n_D^{20} 1.551, d_4^{20} 1.625.

2. Notes

1. Cyclohexene was obtained from Eastman Kodak Company.
2. The 95% orthophosphoric acid is prepared by adding 174 g. (102 ml., 1.5 moles) of 85% phosphoric acid with stirring to 47 g.

of phosphoric anhydride. The solution should be cooled to room temperature before the addition of potassium iodide; otherwise evolution of hydrogen iodide and formation of iodine will take place. After the cyclohexene has been added, the mixture can be heated as desired, since the hydrogen iodide reacts as rapidly as it is generated.

3. Although 95% orthophosphoric acid is recommended for this method, commercial phosphoric acid (85%) may be used, but the reaction proceeds more slowly and the yield is lower.

4. This procedure has been used for the conversion of other olefins to iodides in excellent yield. Yields of 2-iodohexane and 2,3-dimethyl-2-iodobutane from 1-hexene and 2,3-dimethyl-2-butene were 94.5 and 91.4%, respectively.

5. Excess potassium iodide can be recovered by filtering the acid layer, after adding sufficient water to dissolve precipitated inorganic phosphates.

6. If the acid layer has an iodine color, another extraction with 100 ml. of ether is recommended.

3. Methods of Preparation

Iodocyclohexane has been prepared by the action of phosphorus and iodine on cyclohexanol,² and from hydrogen iodide and cyclohexanol,³ chlorocyclohexane,⁴ or cyclohexyl ether.⁵ It has also been prepared by reaction of potassium iodide and chlorocyclohexane.⁶

¹ Ohio State University, Columbus, Ohio.

² Freundler and Damon, *Compt. rend.*, **141**, 593 (1905).

³ Baeyer, *Ann.*, **278**, 107 (1894).

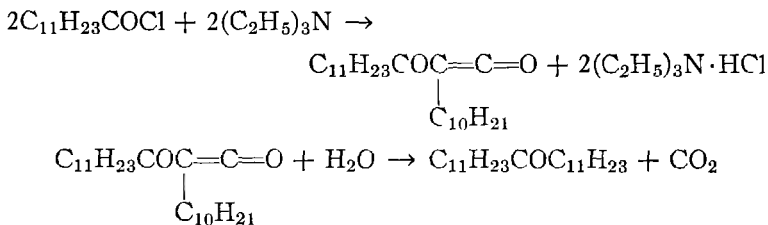
⁴ Markownikoff, *Ann.*, **302**, 12 (1898).

⁵ Lacourt, *Bull. soc. chim. Belg.*, **36**, 353 (1927).

⁶ Conant and Hussey, *J. Am. Chem. Soc.*, **47**, 476 (1925).

LAURONE

(12-Tricosanone)

Submitted by J. C. SAUER.¹

Checked by WILLIAM S. JOHNSON and H. C. DEHM.

1. Procedure

Into a 3-l. three-necked round-bottomed flask fitted with a mechanical stirrer, dropping funnel, and reflux condenser provided with a calcium chloride drying tube is placed 1260 ml. (approximately 900 g.) of anhydrous ether. Stirring is commenced, and 153.0 g. (0.7 mole) of lauroyl chloride (Note 1) is added rapidly through one of the flask openings. The solution is cooled in ice water, and 70.7 g. (0.7 mole) of triethylamine (Note 2) is added over a period of 10 minutes through the dropping funnel in a fine stream. Stirring is discontinued after 1 hour, and the mixture is allowed to come to room temperature. After 12 to 24 hours, the mixture of decylketene dimer (Note 3) and triethylamine hydrochloride is extracted once with 125 ml. of an aqueous 2% sulfuric acid solution to remove the amine salt.

Procedure A. The wet ether layer is transferred to a 3-l. distillation flask and distilled to remove most of the solvent. The warm oily residue is transferred to a 1-l. beaker and mixed with 500 ml. of 2% potassium hydroxide solution. The mixture is heated on a steam bath for 1 hour with occasional stirring and is then chilled in ice water. The waxy cake which settles out on top of the aqueous suspension is skimmed from the surface and dissolved in a mixture of 400 ml. each of acetone and methanol.

The hot solution is filtered through a steam-jacketed funnel and cooled in ice water, and the precipitate is collected on a Büchner funnel with suction. The product is washed on the funnel with cold methanol; after air drying overnight it amounts to 55–65 g. (46–55%), m.p. 62–64°.

Procedure B. The following alternative isolation procedure yields a somewhat purer product. The wet ether layer which has been washed with dilute sulfuric acid to remove amine salt is transferred to a 3-l. distillation flask, 150 ml. of 2% sulfuric acid is added, and the mixture is distilled until nearly all the ether is removed. The hot, oily layer is separated in a separatory funnel and distilled (Note 4). The yield of the fraction distilling at 215–230°/3 mm. is 64–75 g. (54–63%). After recrystallization from 750 ml. of acetone, the laurone weighs 55–65 g. (46–55%), m.p. 68–69° (Note 5).

2. Notes

1. A commercial lauric acid, such as that available from Armour and Company, was converted into the acid chloride by reaction with thionyl chloride. The checkers employed 1 kg. of thionyl chloride for 1201 g. of acid. The product was distilled through a 12-in. Vigreux column, giving 1145 g. (87%) of colorless acid chloride, f.p. -15° to -18° .

2. Triethylamine was purified by the following procedure: fractional distillation, addition of about 2% phenylisocyanate to the distillate, and redistillation.

3. If desired, decylketene dimer can be isolated at this point by filtering the reaction mixture and concentrating the filtrate. The mixture should be handled at all times under anhydrous conditions. The filtration should be carried out by the inverted filtration method.² Difficulties are usually encountered in the filtration step since the amine salt frequently separates as a gel. Seeding the ether solution of lauroyl chloride with triethylamine hydrochloride usually aids in preventing this gel formation. It is necessary to rinse the amine salt several times with ether to extract the dimer, which is usually contaminated with traces of triethylamine hydrochloride.

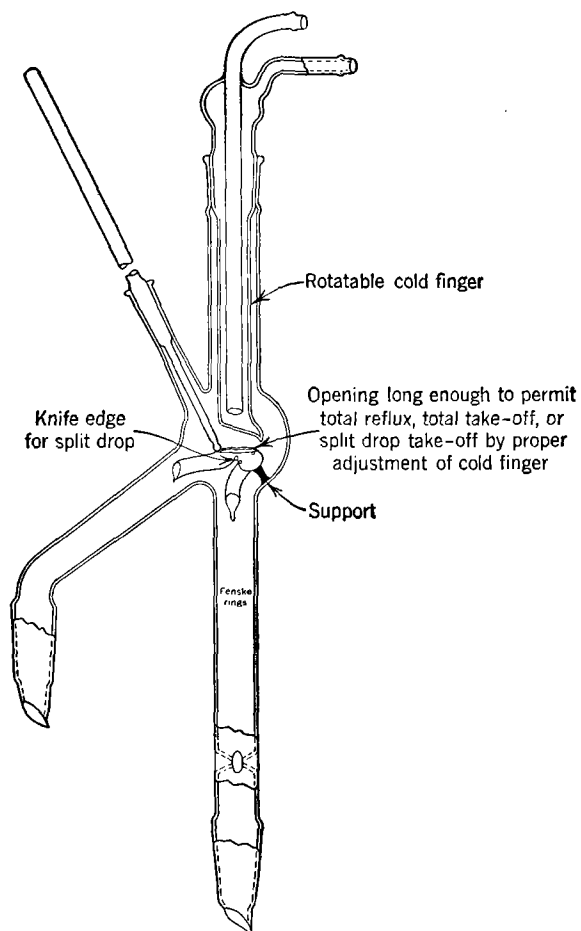


FIG. 1.

4. The electrically heated fractionating column used by the submitter for distilling laurone is pictured in part in Fig. 1. This still, with a column length of 8 in., was designed by Dr. H. J. Sampson of the Rayon Department of E. I. du Pont de Nemours and Company, Inc., Waynesboro, Virginia.

5. Other acid chlorides of the type RCH_2COCl can be similarly dehydrochlorinated. For example, caproyl chloride (1.2 moles) was converted into di-*n*-amyl ketone, b.p. 98–102°/15 mm., in 60–71.5% yield. In this case, it was found preferable to remove the amine salt from the reaction mixture by washing with 2% sulfuric acid. The butylketene dimer was then extracted from the reaction mixture by washing with 5% sodium hydroxide solution; the alkaline solution was acidified with sulfuric acid and steam-distilled. The oily layer in the distillate was separated and fractionated.

3. Methods of Preparation

Laurone has been prepared by hydrating and decarboxylating decylketene dimer.³ It has also been prepared by distilling calcium laurate;⁴ by heating lauric acid with phosphorus pentoxide;⁵ by heating barium laurate under reduced pressure;⁶ by the ester condensation of ethyl laurate with sodium ethoxide⁷ or of methyl laurate with sodium hydride⁸ followed by ketonic hydrolysis; by catalytic ketonization of lauric acid over a chromate catalyst;⁹ or by passing lauric acid over thorium dioxide at 400°.¹⁰

¹ E. I. du Pont de Nemours and Company, Wilmington, Delaware.

² *Org. Syntheses* Coll. Vol. 2, 610 (1943).

³ Sauer, *J. Am. Chem. Soc.*, **69**, 2444 (1947).

⁴ Overbeck, *Ann.*, **84**, 289 (1852).

⁵ Kipping, *J. Chem. Soc.*, **57**, 980 (1890).

⁶ Krafft, *Ber.*, **15**, 1711 (1882).

⁷ Strating, Backer, Lolkema, and Benninga, *Rec. trav. chim.*, **55**, 903 (1936).

⁸ Hansley, U. S. pat. 2,158,071 [C. A., **33**, 6342 (1939)].

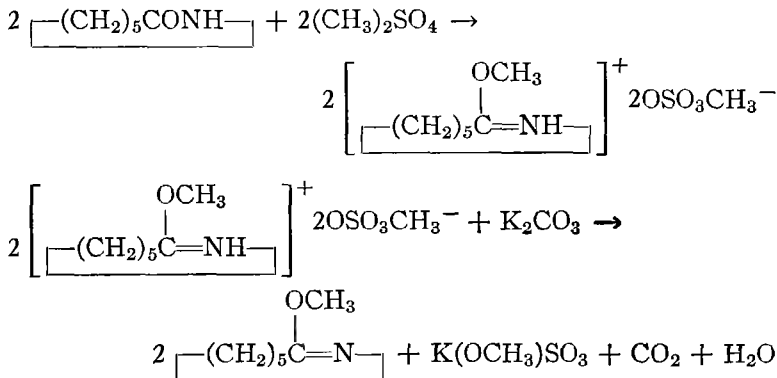
⁹ Wortz, U. S. pat. 2,108,156 [C. A., **32**, 2542 (1938)].

¹⁰ Pickard and Kenyon, *J. Chem. Soc.*, **99**, 57 (1911).

O-METHYLCAPROLACTIM

(2H-Isoazepine, 3,4,5,6-tetrahydro-7-methoxy-)

(ε-Caprolactim, O-methyl)

Submitted by RICHARD E. BENSON and THEODORE L. CAIRNS.¹Checked by CHARLES C. PRICE, KENNETH N. CAMPBELL, and
RICHARD MCBRIDE.

1. Procedure

In a 5-l. three-necked flask equipped with a reflux condenser, a sealed mechanical stirrer, and a 1-l. dropping funnel are placed 678 g. (6.0 moles) of ε-caprolactam ² and 2 l. of benzene (Note 1). The mixture is heated on a steam bath to reflux temperature, during which time all the solid dissolves. At this point 569 ml. (757 g., 6.0 moles) of dimethyl sulfate (Note 1) is added with stirring in a thin stream through the dropping funnel. The rate is about 4 ml. per minute, and the addition requires 2.5 hours. The stirring and heating are continued for an additional 2 hours, during which time two separate phases appear in the reaction mixture. The stirring is then discontinued and the mixture is heated under reflux for an additional 14 hours.

The mixture is cooled to room temperature, and 600 ml. of 50% potassium carbonate is added slowly through the dropping

funnel with stirring (Note 2) to the reaction mixture over a period of 30 minutes. After the vigorous evolution of carbon dioxide has subsided, the mixture is stirred (Note 2) slowly for 30 minutes. The potassium methyl sulfate (Note 3) present is removed by filtration, the solid filter cake is washed with two 100-ml. portions of ether, and the washings are combined with the original filtrate. The filtrate is transferred to a 4-l. separatory funnel, the aqueous layer withdrawn, and the organic layer transferred to a 3-l. round-bottomed flask. The ether and benzene are removed by distillation at slightly reduced pressure (200–600 mm.), and the product distilled through an 8-in. Vigreux column. After a fore-run of benzene and O-methylcaprolactim, the fraction boiling at 65–67°/24 mm., n_D^{25} 1.4610, d_4^{25} 0.9598, is collected. The yield is 450–473 g. (59–62%). An additional quantity of the imino ether can be recovered from the fore-run by distillation through an efficient column, making the total yield 463–517 g. (61–68%) (Note 4).

2. Notes

1. Commercial grade reagents were used throughout. The ϵ -caprolactam was obtained from the Explosives Department, E. I. du Pont de Nemours and Company, Inc., Wilmington, Delaware.

2. Vigorous stirring at this point should be avoided or otherwise an emulsion will be formed that is difficult to break.

3. The solid that separated was not identified, but it was presumed to be potassium methyl sulfate.

4. The corresponding O-ethyl derivative (b.p. 81–82°/26 mm.) can be prepared in 52% yield by a similar procedure.

3. Methods of Preparation

O-Methylcaprolactim has been prepared by the reaction of cyclohexanone oxime, *p*-toluenesulfonyl chloride, and methanol;³ and by the procedure described above, which is a modification of the method given in the patent literature.⁴

¹ E. I. du Pont de Nemours and Company, Inc., Wilmington, Delaware.

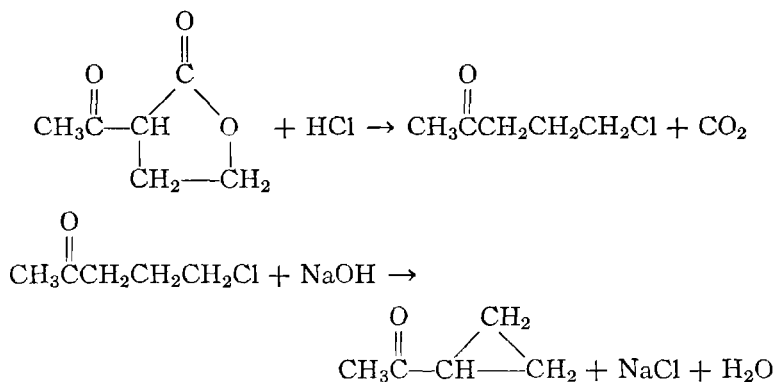
² *Org. Syntheses* Coll. Vol. 2, 371 (1943).

³ Schmidt and Zutavern, Ger. pat. 532,969 [*Frđl.*, 18, 3050 (1931)].

⁴ Schlack, U. S. pat. 2,356,622 [*C. A.*, 39, 1420 (1945)].

METHYL CYCLOPROPYL KETONE

(Ketone, cyclopropyl methyl)



Submitted by GEORGE W. CANNON, RAY C. ELLIS, and JOSEPH R. LEAL.¹

Checked by R. S. SCHREIBER, WM. BRADLEY REID, JR., and
R. D. BIRKENMEYER.

1. Procedure

A. *5-Chloro-2-pentanone*. A mixture of 450 ml. of concentrated hydrochloric acid, 525 ml. of water, and 384 g. (3 moles) of α -acetyl- γ -butyrolactone (Note 1) and a boiling chip are placed in a 2-l. distilling flask fitted with a 90-cm. bulb-type condenser and a receiver immersed in an ice water bath (Note 2). Carbon dioxide is evolved immediately. Heating of the reaction mixture is begun at once, and the temperature is raised at such a rate that the reaction mixture does not foam into the condenser. In about 10 minutes the color changes from yellow to orange to black, the effervescence begins to subside, and distillation commences. The distillation is continued as rapidly as possible

(Note 3). After 900 ml. of distillate has been collected, 450 ml. of water is added to the distilling flask and another 300 ml. of distillate is collected.

The yellow organic layer in the distillate is separated (Note 4), and the aqueous layer is extracted with three 150-ml. portions of ether. The ether extracts are combined with the organic layer and dried for 1 hour over 25 g. of calcium chloride. A saturated calcium chloride layer forms in the bottom. The ether solution is decanted and dried with an additional 25 g. of calcium chloride. The ether is removed by distillation through a 30-cm. column packed with glass helices and fitted with a total condensation, variable take-off head. The residual crude 5-chloro-2-pentanone weighs 287–325 g. (79–90%) (Note 5). When 290 g. of this material is fractionated through a wrapped 12-in. Vigreux column, the major portion boils at 70–72°/20 mm. (n_D^{25} 1.4371) and weighs 258–264 g. (89–91%).

B. *Methyl cyclopropyl ketone*. A 2-l. three-necked flask is fitted with a sweep-type stirrer made from $\frac{1}{4}$ -in. iron rod (Note 6), a reflux condenser, and a 500-ml. dropping funnel. In the flask there is placed a solution consisting of 180 g. (4.5 moles) of sodium hydroxide pellets and 180 ml. of water. To this solution there is added over a period of 15–20 minutes 361.5 g. (342 ml., approximately 3 moles) of the crude 5-chloro-2-pentanone (Note 7). If the reaction mixture does not begin to boil during the addition, boiling is initiated by slight heating of the flask and is continued for 1 hour. Three hundred and seventy milliliters of water is then added slowly to the reaction mixture over a 20-minute period, and the mixture is heated under reflux for an additional hour.

The condenser is arranged for distillation, and a water-ketone mixture is distilled until all the organic layer is removed from the reaction mixture. The aqueous layer of the distillate is saturated with potassium carbonate, and the upper layer of methyl cyclopropyl ketone is separated. The aqueous layer is extracted with two 150-ml. portions of ether. The ether extracts and the ketone layer are combined and dried over 25 g. of calcium chloride for 1 hour. The ether solution is decanted and dried

with an additional 25 g. of calcium chloride. The dried ether solution is fractionated through the 30-cm. column described in Part A (Note 8). The yield of methyl cyclopropyl ketone, b.p. 110–112°, n_D^{25} 1.4226, is 193–210 g. (77–83%).

2. Notes

1. Available from U. S. Industrial Chemicals, Inc. Its preparation has been described by several workers.^{2,3,4}

2. Efficient condensation is important; otherwise some of the product is swept out by the carbon dioxide, and the yield of the chloride is decreased.

3. Any delay in distilling the chloride results in a decrease in yield. If the reaction mixture is allowed to stand overnight before removal of the chloride, the yield is less than 50 %.

4. The chloride is usually the bottom layer. However, occasionally some of it also will be found on top. If so, the addition of 50–100 ml. of ether will cause all the chloride to be in the upper layer and will facilitate separation.

5. Corresponding runs beginning with 128 g. (1 mole) of α -acetyl- γ -butyrolactone gave 107–112 g. (89–93%) of crude 5-chloro-2-pentanone. The checkers consistently obtained yields of 79–81% using U. S. Industrial Chemicals, Inc., lactone.

6. A Hershberg stirrer constructed with a $\frac{1}{4}$ -in. iron or stainless-steel shaft is also satisfactory. Glass stirrers are not recommended because they may break.

7. The use of distilled chloride does not result in better over-all yields.

8. A fractionating column is necessary for the separation of the ether-ketone solution. With an ordinary distilling flask, a ketone-ether mixture, b.p. 41°, is obtained with a resultant decrease in the yield of pure ketone. A well-insulated or preferably heated column is necessary for good fractionation.

3. Methods of Preparation

Methyl cyclopropyl ketone has been prepared from ethyl acetate and ethylene bromide,⁶ and by the action of methylmagnesium bromide on cyclopropyl cyanide.^{6,7} The procedure described for its preparation from 5-chloro-2-pentanone is similar to that of Zelinsky and Dengin.⁸ 5-Chloro-2-pentanone has been prepared by a number of methods.⁹ The procedure given is essentially that of Boon¹⁰ and of Forman.¹¹ A similar procedure has been used for the preparation of the corresponding bromo- and iodo ketones.¹⁰

¹ University of Massachusetts, Amherst, Massachusetts.

² Knunyants, Chelintzev, and Osetrova, *Compt. rend. acad. sci. U.R.S.S.*, [N.S.] **1**, 312 (1934) [*C. A.*, **28**, 4382 (1934)].

³ Matukawa et al., Japan. pat. 134,284 [*C. A.*, **35**, 7421 (1941)].

⁴ Johnson, U. S. pat. 2,443,827 [*C. A.*, **43**, 678 (1949)].

⁵ Freer and Perkin, *J. Chem. Soc.*, **51**, 820 (1887).

⁶ Bruylants, *Rec. trav. chim.*, **28**, 180 (1909) [*C. A.*, **3**, 2700 (1909)].

⁷ Bruylants, *Bull. soc. chim. Belg.*, **36**, 519 (1927) [*C. A.*, **22**, 582 (1928)].

⁸ Zelinsky and Dengin, *Ber.*, **55B**, 3360 (1922).

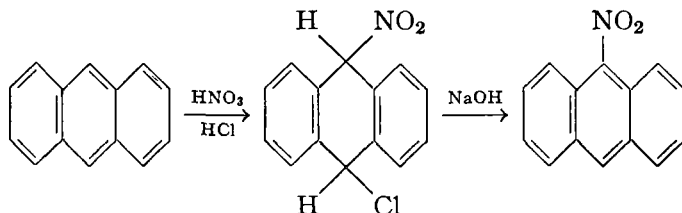
⁹ For a summary with references see Huntress, *Organic Chlorine Compounds*, p. 1274, John Wiley & Sons, New York, New York, 1948.

¹⁰ Boon, U. S. pat. 2,370,392 [*C. A.*, **39**, 4090 (1945)].

¹¹ Forman, U. S. pat. 2,397,134 [*C. A.*, **40**, 4394 (1946)].

9-NITROANTHRACENE

(Anthracene, 9-nitro-)



Submitted by CHARLES E. BRAUN, CLINTON D. COOK,

CHARLES MERRITT, JR., and JOSEPH E. ROUSSEAU.¹

Checked by WILLIAM S. JOHNSON, GEORGE N. SAUSEN, and PAUL R. SHAFER.

1. Procedure

Twenty grams (0.112 mole) of finely powdered anthracene (Note 1) is suspended in 80 ml. of glacial acetic acid (Note 2) in a 500-ml. three-necked round-bottomed flask fitted with a 150-ml. dropping funnel, a thermometer, and an efficient motor-driven stirrer. The flask is immersed in a water bath at 20–25°, and 8 ml. (0.126 mole) of concentrated nitric acid (70% by weight, sp. gr. 1.42), essentially free of oxides of nitrogen, is added slowly from the dropping funnel with vigorous stirring. The rate of addition is controlled so that the reaction temperature does not exceed 30°. About 15–20 minutes is required for this step.

After all the nitric acid is added, the mixture is stirred until a clear solution is obtained (about 30 minutes), and stirring is then continued for an additional 30 minutes. The solution is filtered to remove any anthracene, and a mixture of 50 ml. (0.60 mole) of concentrated hydrochloric acid (37% by weight, sp. gr. 1.19) and 50 ml. of glacial acetic acid is added slowly to the filtrate with vigorous stirring. The pale yellow precipitate of 9-nitro-10-chloro-9,10-dihydroanthracene which forms is separated by suction filtration on a sintered-glass funnel and is washed with two 25-ml. portions of glacial acetic acid and then with water until the washings are neutral. The product is removed from the funnel and triturated thoroughly with 60 ml. of warm (60–70°) 10% sodium hydroxide solution (Note 3). The crude orange nitroanthracene is separated from the warm slurry by suction filtration and is treated with four 40-ml. portions of 10% sodium hydroxide solution (Note 3). The product is finally washed thoroughly with warm water until the washings are neutral to litmus. This treatment requires about 1.5–2 l. of water. The crude 9-nitroanthracene is air-dried and recrystallized from glacial acetic acid (Notes 2 and 4). The yield of bright orange-yellow needles is 15–17 g. (60–70%), m.p. 145–146°.

2. Notes

1. Anthracene of good quality is required. The Eastman Kodak Company product, m.p. 215–217°, is satisfactory, or practical grade anthracene may be purified by codistillation with ethylene glycol.²

2. The checkers employed E. I. du Pont de Nemours and Company, Inc., c.p. acetic acid, which was further purified by distillation from potassium permanganate.

3. The checkers found it desirable to carry out the trituration by grinding the mixture in a mortar, because the nitrochloride has a tendency to form small, hard granules which otherwise may not come in contact with the alkali. The later treatments with alkali may be carried out satisfactorily in a beaker, or directly on the funnel, if thorough mixing is obtained. It is desirable to remove as much of the mother liquor as possible by suction from each of the alkali treatments.

4. For recrystallization, 10 ml. of glacial acetic acid is used for each gram of dried product. It is important that the dissolution be carried out rapidly; otherwise some decomposition may occur, producing anthraquinone as a contaminant. A satisfactory technique is to add the crude, dried, and crushed product rapidly in small portions to the total amount of boiling acetic acid. The solution should then be filtered through a steam-heated funnel.

3. Methods of Preparation

The procedure described is a modification of that of Dimroth.³ 9-Nitroanthracene has also been prepared by nitration of anthracene with copper nitrate in glacial acetic acid and with diacetyl-orthonitric acid.⁴ Other methods include direct nitration in acetic acid solution with nitric acid and acetic anhydride.⁵

¹ University of Vermont, Burlington, Vermont.

² Fieser, *Experiments in Organic Chemistry*, 2nd ed., p. 345, footnote 13, D. C. Heath and Company, Boston, Massachusetts, 1941.

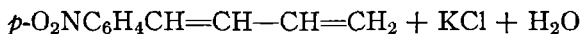
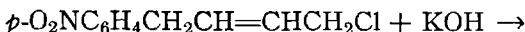
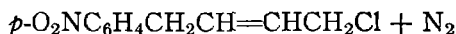
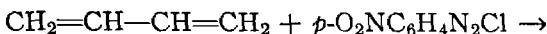
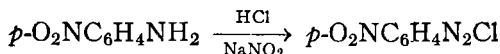
³ Dimroth, *Ber.*, **34**, 221 (1901).

⁴ Braun, Cook, and Rousseau, unpublished work.

⁵ Meisenheimer and Connerade, *Ann.*, **330**, 133 (1904).

1-(*p*-NITROPHENYL)-1,3-BUTADIENE

[1,3-Butadiene, 1-(*p*-nitrophenyl)-]



Submitted by GUS A. ROPP and EUGENE C. COYNER.¹

Checked by ARTHUR C. COPE and DAVID J. MARSHALL.

1. Procedure

A. *1-(p-Nitrophenyl)-4-chloro-2-butene*. *p*-Nitroaniline hydrochloride is prepared by heating 138 g. (1.0 mole) of *p*-nitroaniline (Note 1) with 240 ml. of concentrated hydrochloric acid and 100 ml. of water on a steam bath for 15 minutes with occasional stirring. The mixture is cooled in an ice-salt bath and stirred rapidly in order to precipitate the hydrochloride as fine crystals. Cracked ice (100 g.) is added, and a solution of 70 g. of sodium nitrite is added dropwise with rapid mechanical stirring during a 1-hour period while the temperature of the reaction mixture is held between -4° and $+4.5^\circ$ by cooling with the ice-salt bath. The mixture is stirred for an additional period of 20 minutes and then is filtered through a chilled funnel into an ice-cooled filter flask. The filtrate is kept below 4° (Note 2) and is added through a dropping funnel during 90 minutes to a cold, vigorously stirred mixture composed of 1 l. of acetone, a solution of 80 g. of sodium acetate trihydrate in 100 ml. of water, a solution of 30 g. of cupric chloride in 50 ml. of water, and 130 ml. of liquid butadiene (Note 3). The reaction mixture is kept at -3° to $+2^\circ$ by means of an ice-salt bath while the diazonium salt solution is added. After the addition is completed the cooling

bath is removed and the mixture is stirred for 16 hours. One liter of ether is added, and after several minutes' stirring the ethereal layer is separated, washed with four 1-l. portions of water, and dried over 20 g. of anhydrous magnesium sulfate. The solvent is removed by distillation at 15 mm. by heating on a steam bath, leaving a dark brown oily residue (187–199 g.) of crude 1-(*p*-nitrophenyl)-4-chloro-2-butene (Note 4).

B. 1-(*p*-Nitrophenyl)-1,3-butadiene. The crude 1-(*p*-nitrophenyl)-4-chloro-2-butene obtained in Part A is dissolved in a mixture of 500 ml. of ligroin, b.p. 90–100°, and 500 ml. of benzene; 5 g. of decolorizing carbon is added, and the mixture is heated under reflux for 2 hours. After filtration to separate the decolorizing carbon the solvents are removed by distillation from a steam bath under reduced pressure, and the residual clear oil is dissolved in 400 ml. of methanol. A solution of 112 g. of potassium hydroxide in 600 ml. of methanol is added from a dropping funnel during 30 minutes while the mixture is stirred mechanically and kept at 15–30° by cooling with a bath of cold water. After being stirred for an additional period of 5 minutes the mixture, which contains some precipitated product, is poured into 1.2 l. of cold water. The crude product is collected on a filter, washed well with cold water, and air-dried. It is dissolved in 700 ml. of hot ligroin, b.p. 90–100°, and the solution is treated with 5 g. of decolorizing carbon, and filtered. On cooling, 1-(*p*-nitrophenyl)-1,3-butadiene separates as a yellow crystalline solid which is collected on a filter and dried in a desiccator. The yield of pure product, m.p. 77–79° (Note 5), is 100–108 g. (57–61% based on *p*-nitroaniline).

2. Notes

1. Either a pure grade of *p*-nitroaniline obtained from the Eastman Kodak Company or a technical grade purified by one recrystallization from ethanol was used, m.p. 147.5–148°.

2. The filtrate is kept in an ice-salt bath and transferred to the dropping funnel in small amounts in order to keep the temperature below 4°.

3. Butadiene from a commercial cylinder is passed through an 8-mm. glass tube leading to the bottom of a graduated cylinder cooled with Dry Ice and acetone, where it condenses and is measured as a liquid.

4. The submitters report that small samples of the crude product can be distilled in order to obtain pure 1-(*p*-nitrophenyl)-4-chloro-2-butene, b.p. 160–165°/1 mm.

5. Two recrystallizations from ligroin raise the melting point of the 1-(*p*-nitrophenyl)-1,3-butadiene to a constant value of 78.6–79.4°. The product can be kept for several weeks in a dark bottle at room temperature without evidence of decomposition.

3. Methods of Preparation

1-(*p*-Nitrophenyl)-1,3-butadiene has been prepared only by the method described,² which is an example of the Meerwein reaction (addition of diazonium salts to a carbon-carbon double bond with the elimination of nitrogen).³

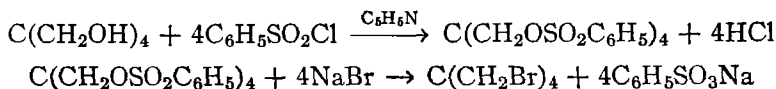
¹ University of Tennessee, Knoxville, Tennessee.

² Coyner and Ropp, *J. Am. Chem. Soc.*, **70**, 2283 (1948).

³ Müller, *Angew. Chem.*, **61**, 179 (1949).

PENTAERYTHRITYL TETRABROMIDE

[Propane, 1,3-dibromo-2,2-bis(bromomethyl)-]



Submitted by HERSEL L. HERZOG.¹

Checked by T. L. CAIRNS and D. W. WOODWARD.

1. Procedure

In a 5-l. three-necked round-bottomed flask equipped with a powerful mechanical stirrer (Note 1), a thermometer, and a 1-l. dropping funnel are placed 130 g. (0.96 mole) of technical penta-

erythritol (Note 2) and 650 ml. of pyridine. The stirrer is started, and to the resulting suspension is added dropwise 750 g. (4.24 moles) of benzenesulfonyl chloride (Note 3) at such a rate that the temperature of the reaction does not rise above 30–35°. The addition requires about 2 hours. The resulting slurry is stirred at 40° for 1 hour after the addition is complete. The slurry is then added slowly (Note 4) to a vigorously stirred solution of 800 ml. of concentrated hydrochloric acid in 1 l. of water and 2 l. of methanol contained in a 9 by 15 in. battery jar. The resulting suspension of granular white pentaerythrityl benzenesulfonate is cooled by addition of 500 g. of ice, filtered with suction, and washed with 5 l. of water and then with 1 l. of cold methanol in two portions.

The crude, slightly wet pentaerythrityl benzenesulfonate is added to 1 l. of diethylene glycol (Note 5) in a 4-l. Erlenmeyer flask equipped with a Hershberg stirrer. Then 600 g. (5.8 moles) of sodium bromide is added, and the mixture is heated in an oil bath at 140–150° with slow stirring (60–120 r.p.m.) overnight. The resulting orange mixture is allowed to cool to about 90°, 2 l. of ice water is added rapidly with stirring, and finally the mixture is cooled to 10° by direct addition of ice. The precipitate is filtered with suction, washed with 2 l. of water, and pressed dry. The yield is 315–323 g. of a crude tan crystalline solid, m.p. 147–149°. The solid is dissolved in 2 l. of boiling acetone and filtered by gravity on a steam-heated funnel. On cooling, the solution deposits colorless glistening plates, which are filtered with suction and washed with 100 ml. of cold 95% ethanol, yielding 150–160 g. of pentaerythrityl tetrabromide, m.p. 159–160° (Note 6). By repeated concentration and cooling of the mother liquor, an additional 90–100 g. of pentaerythrityl tetrabromide, m.p. 156.5–158° (Note 6), is obtained. The combined yield is 228–260 g. (68–78%) (Note 7).

2. Notes

1. A powerful stirrer is necessary to mix the reactants, particularly in the later stages of the reaction when the mixture is

quite viscous. The submitter and checkers used a "Lightnin" stirrer.

2. Heyden Chemical Corporation technical pentaerythritol (Pentek) was found to be satisfactory. It contains about 90% pentaerythritol, the remainder being principally dipentaerythritol.

3. Eastman Kodak Company practical grade benzenesulfonyl chloride was used.

4. Crystallization is extremely slow at first and becomes satisfactory only when the mixture is well seeded. It is well to remove a small portion first and work it up in the hydrochloric acid solution with a spatula to induce crystallization. The mixture should be added slowly at first but more rapidly toward the end.

5. Eastman Kodak Company practical grade diethylene glycol was used.

6. The checkers observed melting points about 2° lower.

7. The yield is based on the assumption that 90% of the starting material is pentaerythritol.

3. Methods of Preparation

The procedure given was developed by Buchman, Herzog, and Fujimoto.² Pentaerythrityl bromide has also been prepared from phosphorus tribromide and pentaerythritol,³ and by the action of hydrobromic acid on pentaerythrityl tetraacetate in acetic acid.⁴

¹ California Institute of Technology, Pasadena, California.

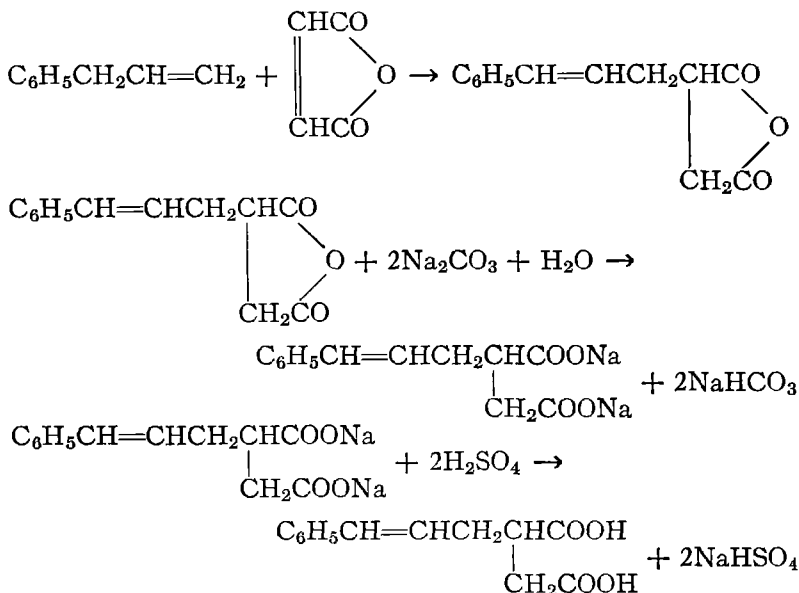
² Buchman, Herzog, and Fujimoto, unpublished results.

³ *Org. Syntheses* Coll. Vol. 2, 476 (1943).

⁴ Perkin and Simonsen, *J. Chem. Soc.*, 87, 860 (1905).

γ -PHENYLALLYLSUCCINIC ACID

(Succinic acid, cinnamyl-)

Submitted by CHRISTIAN S. RONDESTVEDT, JR.¹

Checked by CHARLES C. PRICE and WM. J. BELANGER.

1. Procedure

A mixture of 35.4 g. (0.3 mole) of allylbenzene, 29.4 g. (0.3 mole) of maleic anhydride, and 50 ml. of *o*-dichlorobenzene (Note 1) in a 200-ml. round-bottomed flask is heated under reflux for 22 hours under an air condenser. While the orange mixture cools to 50°, the flask is equipped for vacuum distillation. At a bath temperature below 130°, the solvent and unreacted starting materials are removed by vacuum distillation with a water pump. The boiling range is 66–72°/23 mm. The viscous residue is poured while hot into a 125-ml. sausage flask (Note 2), and the transfer is completed with small amounts of acetone. After

removal of the acetone by vacuum distillation with a water pump, the product is distilled, b.p. $199-206^{\circ}/2$ mm. (bath temperature $220-270^{\circ}$), to give 27–35 g. (42–54%) of a pale yellow liquid which solidifies readily (Note 3).

The product is melted in the receiver and poured into 100 ml. of benzene. An additional 25 ml. of hot benzene is used to rinse the receiver. The benzene solution is brought to boiling, filtered, and diluted with approximately 100 ml. of petroleum ether ($60-75^{\circ}$) until faintly turbid. It is reheated to boiling, allowed to cool, and finally refrigerated for 4 hours. The white crystals are collected on a Büchner funnel, washed with two 25-ml. portions of cold 1:1 benzene-petroleum ether, pressed dry, and air-dried. The yield of anhydride melting at $103-105^{\circ}$ is 24–31 g. (37–47%) (Note 4).

The anhydride is readily hydrolyzed by boiling a mixture of 21.6 g. (0.1 mole) of anhydride, 22.0 g. (0.207 mole) of anhydrous sodium carbonate, and 250 ml. of water for 2 hours on a hot plate. The pale yellow solution is cooled and extracted with 100 ml. of isopropyl ether (Note 5). The ether extract is washed with 50 ml. of water, and the combined water layers are acidified to Congo red by the slow addition of 10% sulfuric acid. The acid separates as an oil which quickly solidifies on cooling and stirring. It is collected on a Büchner funnel, washed with cold water, pressed dry on the funnel, and finally air-dried. The yield is 22 g. (94% based on the anhydride), m.p. $140-143^{\circ}$. The acid is conveniently recrystallized from acetonitrile (Note 6), using 5 ml. per gram of crude acid. The recovery of pure acid having a melting point of $142-143^{\circ}$ is 85% (Note 7).

2. Notes

1. Allylbenzene can be prepared from phenylmagnesium bromide and allyl bromide.² The maleic anhydride used was Eastman Kodak Company white label grade. Slightly higher yields are obtained if it is freshly distilled at 25 mm. Commercial *o*-dichlorobenzene should be distilled before use.

2. A suitable flask is prepared from a 125-ml. distilling flask

by replacing the narrow side arm with a 150-mm. length of 10-mm. tubing. The side arm of a second flask is cut off to 25 mm., and the two flasks are connected by inserting the 10-mm. side arm into the bulb of the second flask.

A few boiling stones or sticks are added to the first flask containing the material to be distilled, a rubber stopper bearing a thermometer is inserted, and vacuum is applied to the shortened side arm of the receiver.

3. A Wood's metal bath is convenient as a high-temperature heat source.

4. Once-crystallized anhydride is sufficiently pure for conversion to the acid. A second recrystallization gives pure material, m.p. 106.0–106.5°.

5. Ethyl ether may be used. The aqueous layers must then be heated to boiling and cooled before acidification; otherwise the acid is slow to crystallize.

6. Acetonitrile is most convenient, but ethanol, aqueous acetic acid, or aqueous dioxan may be used.

7. The acid is partially dehydrated near its melting point. The reported melting point was observed by immersing the capillary at 140° and heating at 2° per minute.

3. Method of Preparation

γ -Phenylallylsuccinic anhydride and the derived acid have been prepared by heating maleic anhydride with excess allylbenzene in an autoclave at 170–175° for 24 hours.³ The above procedure is more convenient since an autoclave is unnecessary.

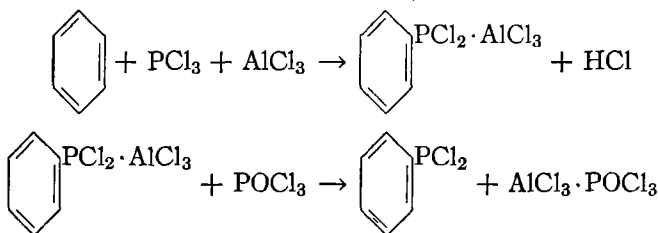
¹ University of Michigan, Ann Arbor, Michigan.

² Hershberg, *Helv. Chim. Acta*, **17**, 351 (1934).

³ Alder, Pascher, and Schmitz, *Ber.*, **76**, 27 (1943).

PHENYLDICHLOROPHOSPHINE

(Phosphine, dichlorophenyl-)



Submitted by B. BUCHNER and L. B. LOCKHART, JR.¹

Checked by CLIFF S. HAMILTON and P. J. VANDERHORST.

1. Procedure

In an all-glass apparatus consisting of a 1-l. three-necked flask equipped with a long-stem thermometer, a rubber-sealed mechanical stirrer, and a suitable condenser (Note 1) are placed 165 g. (1.2 moles) of phosphorus trichloride, 23.4 g. (0.3 mole) of benzene, and 53 g. (0.4 mole) of anhydrous aluminum chloride. The mixture is stirred continuously and heated (Note 2). As the temperature increases, the mixture becomes a homogeneous yellow solution and begins to reflux. After 2 hours, the reaction mixture is heated under reflux as vigorously as possible (Note 3). At the end of the third hour, the evolution of hydrogen chloride has almost ceased. The heat source is removed, and, while the mixture is still hot, 62 g. (0.4 mole) of phosphorus oxychloride is added gradually (Note 4) from a dropping funnel (Note 5). The granular precipitate of aluminum chloride-phosphorus oxychloride complex settles rapidly. After the apparatus is disassembled, 6-8 petroleum ether extractions of 100 ml. each are performed to remove phenyldichlorophosphine and the unreacted starting materials from the reaction flask. The residue is transferred to a Büchner funnel and washed with several small portions of petroleum ether, and the combined extracts and washings

are concentrated under reduced pressure. Crude phenyldichlorophosphine is removed by distilling to dryness under reduced pressure and is purified by fractionating through a satisfactory column (Note 6). The product distils at 68–70°/1 mm. (90–92°/10 mm.), n_D^{25} 1.5962 (Note 7), and weighs 38.5–42 g. (72–78%) (Note 8).

2. Notes

1. The submitters and checkers used a Friedrich condenser. The condenser outlet was connected to a gas absorption trap filled with sodium hydroxide solution to neutralize escaping acid vapors. A tube filled with Drierite was inserted between the condenser and trap to absorb moisture which might diffuse from the trap.

2. Slow heating is desirable to prevent too rapid evolution of hydrogen chloride.

3. Cold water, approximately 0°, is circulated by means of a water pump in order to increase the efficiency of the condenser.

4. The reaction between phosphorus oxychloride and aluminum chloride is exothermic.

5. The thermometer is replaced by a dropping funnel.

6. The submitters and checkers employed a 20-cm. column packed with glass helices.

7. The checkers obtained an average value of n_D^{24} 1.5919.

8. According to the submitters, *p*-tolylidichlorophosphine, *p*-ethylphenyldichlorophosphine, and *p*-isopropylphenyldichlorophosphine may be prepared by this general procedure in yields of 66%, 69%, and 64%, respectively.

3. Methods of Preparation

Phenyldichlorophosphine has been prepared by the vapor-phase reaction of benzene and phosphorus trichloride over pumice in a hot tube² and by the action of diphenylmercury on phosphorus trichloride.³ The method described here is a Michaelis modification of a Friedel-Crafts reaction.⁴

¹ Naval Research Laboratory, Washington, D. C.

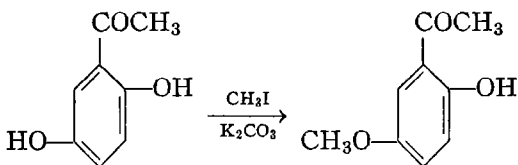
² Michaelis, *Ber.*, **6**, 601 (1873).

³ Michaelis, *Ann.*, **181**, 288 (1876).

⁴ Michaelis, *Ber.*, **12**, 1009 (1879).

QUINACETOPHENONE MONOMETHYL ETHER

(Acetophenone, 2-hydroxy-5-methoxy-)



Submitted by G. N. VYAS and N. M. SHAH.¹

Checked by WILLIAM S. JOHNSON and R. T. KELLER.

1. Procedure

In a 1-l. round-bottomed flask fitted with a reflux condenser and a calcium chloride guard tube are placed 30.0 g. (0.197 mole) of quinacetophenone ² (Note 1) and 300 ml. of acetone (Note 2). The mixture is warmed on a steam bath to dissolve the quinacetophenone. The resulting greenish solution is cooled to room temperature under tap water, and 28 g. (0.20 mole) of anhydrous potassium carbonate is added followed by 42 g. (0.295 mole) of methyl iodide. The mixture is allowed to reflux on a water bath at 60–70° for about 6 hours (Note 3).

As much of the acetone as possible is removed by distillation on the water bath (Note 4), and the residual dark-colored liquid is cooled and acidified with 2 *N* sulfuric acid with cooling under the water tap. The resulting mixture is steam-distilled until no oily drops are seen collecting in the condenser. The distillate, which amounts to about 2.5 l., is allowed to stand overnight at room temperature, and the greenish crystals are separated by suction filtration, washed twice with cold water, and air-dried.

The yield of quinacetophenone monomethyl ether, m.p. 48–50°, is 18–21 g. (55–64%) (Note 5).

The brown solution remaining in the distilling flask is filtered while hot; on being cooled it gives 6–7 g. of brownish needles of crude quinacetophenone.

2. Notes

1. The quinacetophenone² is dried in an oven at 100–110° for 2–3 hours.

2. The acetone is dried over anhydrous potassium carbonate and distilled.

3. The temperature of the water bath should not exceed 70°; otherwise serious bumping may occur.

4. The recovered acetone may be reused for another methylation.

5. The submitters state that the *dimethyl* ether of quinacetophenone is conveniently prepared by the following procedure: In a 1-l. round-bottomed flask fitted with a reflux condenser 60 g. (0.39 mole) of quinacetophenone² is dissolved in 300 ml. of ethanol by heating. The source of heat is then removed, and to the hot solution are alternately added in five installments with shaking a solution of sodium hydroxide (40 g. in 100 ml. of water) and dimethyl sulfate (120 g.). The heat evolved during the reaction makes the solution boil. After the addition is complete (about 20 minutes), the reaction mixture is made alkaline by the further addition of 10 g. of sodium hydroxide in 20 ml. of water and is allowed to reflux on the water bath for 3 hours. The dark mixture is distilled to remove most of the ethanol, and the residual liquid in the flask is steam-distilled. The distillate, which amounts to about 2.5 l., is cooled in an ice bath and saturated with sodium chloride, whereupon a thick oil settles to the bottom. Most of the aqueous layer is decanted, and the remaining oil is extracted with ether and dried over calcium chloride. The ether is removed by distillation, and the residue is fractionated at reduced pressure to give 50–52 g. (71–74% yield) of material boiling at 152–156°/15 mm., m.p. 20–22°.

3. Methods of Preparation

Quinacetophenone monomethyl ether has been prepared by the methylation of quinacetophenone with dimethyl sulfate and alkali,³ and by the partial demethylation of quinacetophenone dimethyl ether.⁴ It has also been obtained as a by-product in the preparation of quinacetophenone dimethyl ether.⁵

¹ M. R. Science Institute, Gujarat College, Ahmedabad, India.

² *Org. Syntheses*, **28**, 42 (1948).

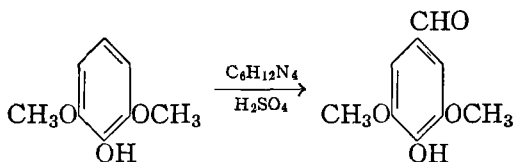
³ Kostanecki and Lampe, *Ber.*, **37**, 774 (1904).

⁴ Baker, Brown, and Scott, *J. Chem. Soc.*, **1939**, 1926.

⁵ Kauffmann and Beisswenger, *Ber.*, **38**, 792 (1905).

SYRINGIC ALDEHYDE

(Syringaldehyde)



Submitted by C. F. H. ALLEN and GERHARD W. LEUBNER.¹

Checked by R. S. SCHREIBER, WM. BRADLEY REID, JR., and R. W. JACKSON.

1. Procedure

A well-stirred (Notes 1 and 2) mixture of 740 ml. of glycerol and 216 g. of boric acid, in a 2-l. three-necked round-bottomed flask fitted with a thermometer and a condenser for downward distillation, is dehydrated by heating in an oil bath to *exactly* 170°. This temperature is maintained for 30 minutes and then allowed to drop. When the temperature has fallen to 150°, a mixture of 154 g. (1 mole) of pyrogallol-1,3-dimethyl ether and 154 g. (1.1 moles) of hexamethylenetetramine (Note 3) is added as rapidly as possible through the neck holding the thermometer. The temperature drops to approximately 125°. Rapid heating

is immediately started but is slowed down when the temperature begins to reach 145° and stopped at 148° . The reaction must be watched and controlled *very carefully* when this temperature is reached, since the reaction becomes exothermic at this point (Notes 4, 5, and 6). The temperature is maintained at 150 – 160° for approximately 6 minutes (Note 7). At the end of this reaction time the mixture is cooled to 110° as rapidly as possible (Notes 6 and 8), and a previously prepared solution of 184 ml. of concentrated sulfuric acid in 620 ml. of water is added to the reaction mixture. After being stirred for 1 hour, the mixture is cooled to 25° in an ice bath. The boric acid, which separates from the solution, is removed by filtration (Note 9) and washed free of mother liquor with 400 ml. of water. The filtrate and washings are combined and extracted with three 500-ml. portions of chloroform (Notes 10, 11, and 12).

The chloroform solution is then extracted with a filtered solution of 180 g. of sodium bisulfite in 720 ml. of water (Note 13) by stirring rapidly with a Hershberg stirrer for 1 hour. The separated bisulfite solution is washed twice with chloroform, filtered, and acidified in a hood with a solution of 55 ml. of concentrated sulfuric acid in 55 ml. of water. After careful heating on a steam bath for a short time, air is bubbled through the hot solution until all the sulfur dioxide has been expelled. The product, which separates as a mixture of crystals and oil, readily solidifies upon cooling (Note 14). The syringic aldehyde is collected by filtration, washed with cold water, and dried in an oven at 40° to give 62.5–66 g. of light-tan material, melting at 110.5 – 111° , which still contains a small amount of foreign material that does not melt at 300° . Recrystallization of the crude product from aqueous methanol using 30 ml. of water and 3 ml. of methanol for each 10 g. of aldehyde gives 56–59 g. (31–32%) of product melting clear at 111 – 112° (uncor.). A second extraction of the chloroform solution with a filtered solution of 60 g. of sodium bisulfite in 240 ml. of water gives an additional 3–4 g. of product.

2. Notes

1. The use of a Hershberg ² stirrer is recommended.
2. It is desirable to conduct this preparation in a hood because of the large volume of ammonia liberated in the second step.
3. Eastman Kodak Company white label grade pyrogallol-1,3-dimethyl ether was used. A larger excess of hexamethylene-tetramine in a small trial run did not improve the yield.
4. The reaction mixture darkens rapidly, and there is a vigorous evolution of ammonia.
5. The temperature usually rises to 160° within 5 minutes, and cooling is necessary.
6. Cooling is accomplished by playing a stream of cold water over the outside of the flask.
7. There is undoubtedly some leeway in these conditions. The same yields were obtained when the temperature was maintained at 150–160° for periods of 5 to 9 minutes. Longer reaction times, without rapid cooling after the heating period, lowered the yield. Reaction times of 15 minutes, 30 minutes, and 1 hour gave yields of 20.8%, 10.0%, and 6.5%, respectively. Liggett and Diehl,³ after having run a large number of other Duff reactions, have come to the conclusion that the temperature may vary between 145° and 175° without detriment to the yield.
8. About 3 to 5 minutes is required for cooling.
9. If not removed, the boric acid makes extraction of the product impossible or very difficult. Since the boric acid is finely divided, filtration is extremely slow unless large Büchner funnels, preferably with large holes, are employed. The checkers avoided the difficulty by using a filter cloth at this point.
10. The product cannot be isolated by steam distillation of the reaction mixture.
11. Syngic aldehyde is much more soluble in chloroform than in ether. Extraction is essentially complete since a fourth extraction gave only a 0.3–0.7% increase in yield.
12. If the aldehyde is isolated directly by concentration of the

chloroform solution, the color is darker, and the melting point and yield are lower.

13. This represents a large excess of sodium bisulfite, but smaller amounts remove a smaller percentage of the syringic aldehyde from the chloroform solution. When larger amounts of bisulfite are employed, extraction of the product is still incomplete.

14. The product should be cooled to just 15° and filtered immediately. Longer and further cooling causes sodium sulfate to crystallize from the mixture. Very little product remains in the filtrate.

3. Methods of Preparation

This procedure is a modification of the method described by Manske and coworkers.⁴ Syringic aldehyde has also been obtained by numerous other procedures from pyrogallol-1,3-dimethyl ether^{5, 6, 7, 8} and from gallic acid.^{9, 10, 11}

¹ Eastman Kodak Company, Rochester, New York.

² *Org. Syntheses Coll. Vol. 2*, 117 (1943).

³ Liggett and Diehl, *Proc. Iowa Acad. Sci.*, **52**, 191 (1945).

⁴ Manske, Ledingham, and Holmes, *Can. J. Research*, **23B**, 100 (1945).

⁵ Graebe and Martz, *Ber.*, **36**, 1031 (1903).

⁶ Pauly and Strassberger, *Ber.*, **62**, 2277 (1929).

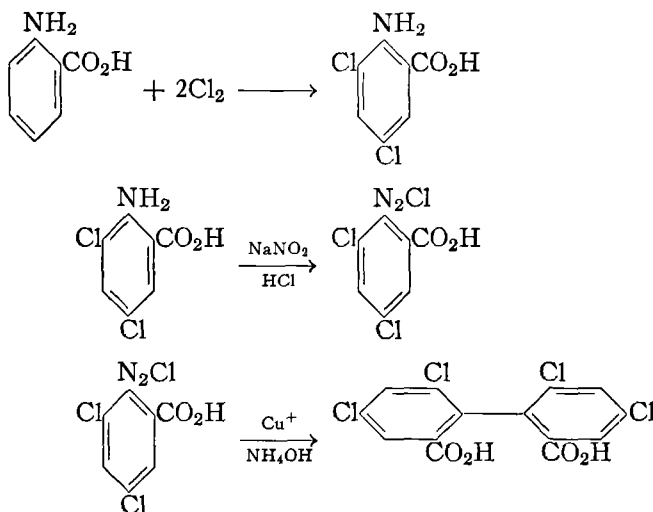
⁷ Pearl, *J. Am. Chem. Soc.*, **70**, 1746 (1948).

⁸ Mauthner, *Ann.*, **395**, 273 (1913).

⁹ Mauthner, *J. prakt. Chem.*, **142**, 26 (1935).

¹⁰ McCord, *J. Am. Chem. Soc.*, **53**, 4181 (1931).

¹¹ Sharp, *J. Chem. Soc.*, **1937**, 852.

dl*-4,4',6,6'-TETRACHLORODIPHENIC ACID*(*dl*-Diphenic acid, 4,4',6,6'-tetrachloro-)**

Submitted by EDWARD R. ATKINSON, DONALD M. MURPHY, and
JAMES E. LUFKIN.¹

Checked by R. S. SCHREIBER, WM. BRADLEY REID, JR., and
R. D. BIRKENMEYER.

1. Procedure

A. 3,5-Dichloro-2-aminobenzoic acid. A solution of 45 g. (0.33 mole) of anthranilic acid, 150 ml. of concentrated hydrochloric acid, and 850 ml. of water is placed in a 2-l. three-necked flask in a hood and weighed. While the solution is rapidly stirred, chlorine is introduced until the reaction mixture gains 45 g. (0.63 mole) in weight (Note 1). The flask is surrounded by a water bath to maintain the temperature of the reaction mixture below 30° during the chlorination procedure. The reaction mixture is filtered by suction, using a large (10–12 in.) Büchner funnel; the crude product is washed with water and then dried at room temperature (Note 2). There is obtained 55–65 g. of

crude product melting at about 205°. The crude product is leached with 4 ml. of boiling benzene per gram, filtered by suction, and washed on the filter with 1 ml. of cold benzene per gram. After drying at room temperature, there is obtained 46.5–53 g. (69–77%) of crude 3,5-dichloro-2-aminobenzoic acid. The melting point of this material should not be lower than 211° (Notes 3 and 4).

B. *Diazotization of 3,5-dichloro-2-aminobenzoic acid.* Fifty grams (0.24 mole) of 3,5-dichloro-2-aminobenzoic acid is dissolved in a solution of 12 g. (0.3 mole) of sodium hydroxide in 700 ml. of water. To this solution is added 20 g. (0.29 mole) of sodium nitrite, and the solution is cooled to 10° (Note 5). One hundred milliliters of concentrated hydrochloric acid (sp. gr. 1.191) and 200 ml. of water are placed in a 2-l. three-necked flask and cooled to 10°. The cold solution of sodium 3,5-dichloro-2-aminobenzoate and sodium nitrite is then added to the hydrochloric acid solution with cooling (10°) and efficient stirring at such a rate that no appreciable accumulation of undiazotized amine results (Note 6). At the conclusion of the diazotization, the resulting solution is stirred a few minutes with 2 g. of diatomaceous earth and filtered by suction (Note 7).

C. *Preparation of the reducing agent.* One hundred and twenty-five grams (0.5 mole) of cupric sulfate pentahydrate is dissolved in 500 ml. of water contained in a 3-l. three-necked flask equipped with a mechanical stirrer, and then 210 ml. of concentrated ammonium hydroxide (sp. gr. 0.90) is added with stirring. The solution is cooled to 10°. A solution of 40 g. (0.575 mole) of hydroxylamine hydrochloride in 140 ml. of water is prepared and also cooled to 10°. To the hydroxylamine hydrochloride solution there is added 95 ml. of 6 N sodium hydroxide solution, and if not entirely clear, it is filtered by suction. This hydroxylamine solution is immediately added to the ammoniacal cupric sulfate solution with stirring. Reduction occurs at once with the evolution of nitrogen, and the solution becomes pale blue. If this solution is not used at once, it should be protected from the air.

D. *dl-4,4',6,6'-Tetrachlorodiphenic acid.* The reducing solution prepared above is cooled to 10° and maintained at 10–15° during

the addition of the diazo solution from Part B, which is added from a dropping funnel. A feed tube having a 2-mm. opening and dipping well below the surface of the reducing solution should be attached to the stem of the dropping funnel. The feed tube should be bent upward at the end and so placed that mixing of the reducing solution occurs rapidly (Note 8). The diazo solution is added at approximately 25 ml. per minute, and excessive foaming is suppressed by the addition of small amounts of ether (Note 9). At the conclusion of the reaction (Note 10), the ammoniacal solution is transferred to two 4-l. beakers, heated to 80–90°, and rapidly acidified to litmus with concentrated hydrochloric acid with vigorous stirring (Note 11). At this point acidification is continued more carefully until the solution is acid to Congo red (Note 12). A total excess of 100 ml. of acid is then added, and the solution is allowed to stand overnight. The product is filtered by suction and washed on the filter with four 250-ml. portions of water. After drying, the yield of crude product, melting at 180–215°, is 29–38.5 g. (63–84%).

The crude product is dissolved in 3.5 ml. of concentrated sulfuric acid per gram, heated with stirring to 150° for 5 minutes, and allowed to cool overnight. The resulting product is filtered by suction through a sintered-glass funnel and washed on the filter with three 15-ml. portions of concentrated sulfuric acid at room temperature. The filter cake is removed from the funnel and boiled with 50 ml. of water to remove adherent sulfuric acid. The product is then filtered and dried. The above procedure yields 19–22 g. (42–48%) of almost colorless *dl*-4,4',6,6'-tetrachlorodiphenic acid melting at 243–250° (uncor.) (Note 13). Pure acid may be obtained by a second recrystallization from concentrated sulfuric acid. Twenty grams of crude *dl*-4,4',6,6'-tetrachlorodiphenic acid, m.p. 243°, recrystallized from 70 ml. of concentrated sulfuric acid yields 6.54 g. (33% recovery) of colorless product melting at 258–259°.

2. Notes

1. The rate of flow of chlorine is adjusted so that the reaction mixture is saturated with gas and some gas escapes from the surface of the solution. An indication of proper duration of chlorination is the development of a distinct brown color in the suspension. Further chlorination leads to a decrease in yield with the formation of polychloro products.² The time required for chlorination is about 1 hour.

2. Drying at elevated temperatures gives an inferior product because of the formation of polychloro by-products at this stage.

3. Pure 3,5-dichloro-2-aminobenzoic acid ³ has a melting point of 231°. The product described here is adequate for the subsequent step.

4. This procedure can be performed using 10 times the quantities specified. The chlorination is carried out in a jar having a capacity of 12–14 l. Chlorine is introduced by means of a copper tube coiled at the bottom of the jar and perforated in several places. The time of chlorination is 2 hours. The percentage yield is the same as that for the scale described above.

5. This solution is almost saturated with the sodium salt of 3,5-dichloro-2-aminobenzoic acid. If crystallization occurs, additional water may be added. Obviously, temperatures below 10° should be avoided.

6. As the salt solution enters the acid solution, there is a momentary precipitation of the amino acid, which dissolves rapidly as it is diazotized. The checkers found that this addition took about 2 hours.

7. The diazo solution may be stored as long as 1 day at 10–15°. The insoluble gelatinous material that forms during storage should be removed by filtration just before use. The filter flask used at this point should be cooled in an ice bath to prevent further decomposition of diazo solution.

8. This trap arrangement prevents premature reaction of the entering diazo solution with ammonia, which otherwise would be carried up the feed tube by ascending bubbles of nitrogen.

9. The rate of addition is not a critical factor. More rapid addition requires more vigorous stirring and may lead to troublesome foaming.

10. The solution may stand for a week before being used.

11. The checkers recommend the use of a Hershberg stirrer.

12. Basic copper salts which precipitate during the acidification redissolve before the Congo red end point is reached if the later stages of acidification are performed carefully with adequate stirring.

13. This procedure is adaptable to 10 times the quantities specified here. Diazotization is carried out in a 12-l. jar. The diazo solution is allowed to stand overnight to facilitate the separation, by decantation or siphoning, of the non-diazotizable impurities whose large-scale filtration is tedious. The main synthesis is performed in a carboy having a capacity of not less than 30 l. The metal stirrer is protected by a coat of paraffin wax. Several addition tubes are used for the diazo solution. By adding appropriate quantities of ice, the necessity of external cooling for these large vessels is avoided. The yield is 39-42% of material melting at 244-250°.

3. Methods of Preparation

3,5-Dichloro-2-aminobenzoic acid can be prepared by the chlorination of anthranilic acid in glacial acetic acid solution ³ and by the action of sulfuryl chloride on anthranilic acid.^{4,5} The above procedure is derived from a more recent detailed study of the chlorination reaction.²

The above procedure is derived from the work of Atkinson and Lawler ⁶ but employs a more suitable reducing agent than that ⁷ previously used to convert diazotized anthranilic acid to diphenic acid. The product can be resolved into its optically active forms,⁶ which are stable to racemization.

¹ University of New Hampshire, Durham, New Hampshire.

² Atkinson and Mitton, *J. Am. Chem. Soc.*, **69**, 3142 (1947).

³ Elion, *Rec. trav. chim.*, **44**, 1106 (1925).

⁴ Eller and Klemm, *Ber.*, **55**, 222 (1922).

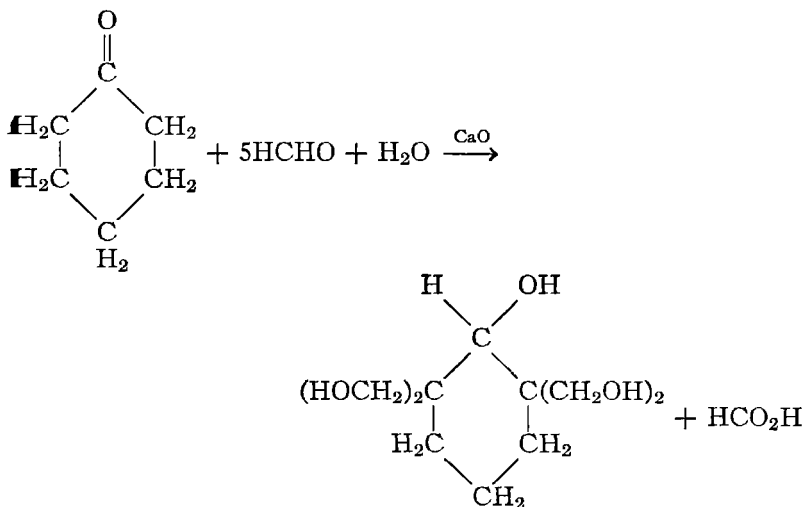
⁵ Durrans, *J. Chem. Soc.*, **123**, 1424 (1923).

⁶ Atkinson and Lawler, *J. Am. Chem. Soc.*, **62**, 1704 (1940).

⁷ *Org. Syntheses* Coll. Vol. **1**, 222 (1941).

2,2,6,6-TETRAMETHYLOLCYCLOHEXANOL

[Cyclohexanol, 2,2,6,6-*tetrakis*(hydroxymethyl)-]



Submitted by HAROLD WITTCOFF.¹

Checked by R. S. SCHREIBER, WM. BRADLEY REID, JR., and JOHN L. WHITE.

1. Procedure ²

A mixture of 196 g. (206 ml., 2 moles) of freshly distilled cyclohexanone, 332 g. (11 moles) of 99.5% paraformaldehyde (Note 1), and 1.8 l. of water is placed in a 5-l. flask equipped with a thermometer and an efficient stirrer. The mixture is cooled to 10–15° by an ice-water bath, and 70 g. (1.25 moles) of calcium oxide is added through a powder funnel over a period of 10–15

minutes. The temperature is allowed to rise slowly to 40° and is kept there by means of the cooling bath until the addition is complete. Stirring is maintained throughout. The reaction mixture is stirred for an additional 30 minutes. During this time the temperature usually falls to approximately 35°, and at this point the cooling bath is removed. The reaction mixture is then made slightly acid (pH 6–6.5) by the addition of 11–13 ml. of aqueous 87% formic acid. It is best to stir the reaction mixture for 30 minutes after neutralization in order to make sure that any suspended particles of lime are neutralized. If at the end of this time the solution is not acid, more formic acid should be added. The reaction mixture is then evaporated under reduced pressure to dryness (Note 2). The residue, which consists of a mixture of product and calcium formate, is mixed with 1 l. of absolute methanol. On warming, the organic material dissolves and the calcium formate settles to the bottom of the flask. A practically colorless solution of the product is obtained by filtration with suction (Note 3) through a heated funnel. The insoluble calcium formate is washed with about 50 ml. of methanol. Approximately one-half of the methanol is removed under reduced pressure, and the residual syrupy solution (Note 4) is allowed to crystallize in an ice chest for 24 hours. Thereafter the product is filtered and washed with 50 ml. of methanol. The mother liquor and washings are combined and set aside. With a mortar and pestle, the crystals are triturated successively with three 200–300-ml. portions of acetone, filtered, and air-dried. By continued evaporation of the mother liquor and washings, at least two successive crops of product are obtained, and these are processed as described above (Note 5). The total yield of product melting at 128–129° is 320–374 g. (73–85%). Recrystallization of 100 g. of material, m.p. 128–129°, from 175 ml. of absolute methanol yields 84 g. of pure product melting at 129–130°.

2. Notes

1. An equivalent quantity of aqueous formaldehyde free from methanol may be used.

2. The evaporation may be carried out in an ordinary distillation apparatus, but it is essential to stir the mixture to prevent bumping. It is advantageous from the point of view of speed and convenience to employ the method described below.

A 3-l. three-necked flask is fitted with an efficient rubber-sealed stirrer, an upright steam-heated condenser, the upper end of which is joined to a separatory funnel, and an outlet tube connected to a long water-cooled condenser placed for downward distillation. The end of this condenser is fitted to a 2-l. two-necked flask which is connected to a good water pump and immersed in an ice bath. The apparatus, with the exception of the separatory funnel, is placed under vacuum. The aqueous solution contained in a separatory funnel is slowly passed through the upright condenser into the three-necked flask heated on a steam bath. The syrupy residue collects in the flask, and the water vapor is removed through the condenser fitted for downward distillation. The residue is heated until no more water is removed. The total time required to strip off the water is 30 to 60 minutes.

3. The checkers found that suction filtration was very slow, owing to the very finely divided material that collected on the funnel. This was corrected by adding a filtering aid (Celite) to the crude mixture and filtering by suction, using an ordinary Büchner funnel (6-in. size). After removal of the solid by suction filtration, the methanol volume was reduced as indicated.

4. The submitter reported that it was preferable to carry out the crystallizations in metal beakers since the crystals were very hard to remove without breakage, but the checkers experienced no such difficulty.

5. Runs employing six times the quantities specified here have been carried out in 22-l. flasks with similar results.

3. Methods of Preparation

2,2,6,6-Tetramethylolcyclohexanol has been prepared by Manich and Brose ³ by condensing cyclohexanone with formaldehyde

in the presence of calcium oxide and precipitating the catalyst as calcium sulfate.

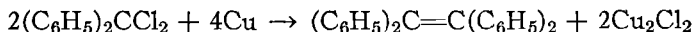
¹ General Mills, Inc., Minneapolis, Minnesota.

² This procedure forms a portion of the subject matter of U. S. pat. 2,462,031 [C. A., **44**, 656 (1950)]; U. S. pat. 2,493,733 [C. A., **44**, 3017 (1950)].

³ Mannich and Brose, *Ber.*, **56**, 833 (1923).

TETRAPHENYLETHYLENE

(Ethylene, tetraphenyl-)



Submitted by ROBERT E. BUCKLES and GEORGE M. MATLACK.¹

Checked by T. L. CAIRNS and C. J. ALBISETTI.

1. Procedure

A solution of 75 g. (0.32 mole) of diphenyldichloromethane (Note 1) in 250 ml. of anhydrous benzene is placed in a 500-ml. round-bottomed flask fitted with a reflux condenser. To the solution is added 50 g. (0.78 gram atom) of powdered copper (Note 2). The mixture is boiled gently for 3 hours. The hot solution is filtered, and 250 ml. of absolute ethanol is added to the filtrate. On cooling 25–31 g. (47–60%) of light yellow crystals, m.p. 222–224°, are obtained. The mother liquor is concentrated to about 200 ml. by distillation from a 1-l. Claisen flask. Cooling the residue yields 6–12 g. of yellow product. Crystallization of this crude material from a 1:1 by volume mixture (12 ml. for each gram) of absolute ethanol and benzene gives an additional 2.5–10 g. of tetraphenylethylene, m.p. 223–224°. The total yield is 29–37 g. (55–70%).

2. Notes

1. Diphenyldichloromethane is conveniently prepared from benzophenone and phosphorus pentachloride.² A product of b.p. 180–181°/17 mm. is obtained in about 90% yield.

2. The checkers used bronze powder obtained from George Benda, Inc., Boonton, New Jersey. Some varieties of copper powder tended to form a dense paste which did not disperse readily and resulted in lower yields.

3. Methods of Preparation

This procedure is adapted from the method of Schlenk and Bergmann.³ Tetraphenylethylene has been prepared by the reaction of diphenylmethane with diphenyldichloromethane;⁴ by the reaction of diphenyldichloromethane with silver or zinc;⁴ by the reaction of thiobenzophenone with copper;⁵ by the reaction of diphenylmethane with sulfur;⁶ by the reduction of benzophenone with amalgamated zinc in the presence of hydrochloric acid;⁷ and by the rearrangement of 1,2,2,2-tetraphenylethanol with acetyl chloride.⁸

¹ The State University of Iowa, Iowa City, Iowa.

² *Org. Syntheses* Coll. Vol. 2, 573 (1943).

³ Schlenk and Bergmann, *Ann.*, **463**, 1 (1928).

⁴ Norris, Thomas, and Brown, *Ber.*, **43**, 2958 (1910).

⁵ Schönberg, Shütz, and Nickel, *Ber.*, **61**, 1375 (1928).

⁶ Ziegler, *Ber.*, **21**, 779 (1888).

⁷ Steinkopf and Wolfram, *Ann.*, **430**, 113 (1923).

⁸ Lévy and Lagrave, *Bull. soc. chim. France*, [4] **43**, 437 (1928).

THIOLACETIC ACID

(Acetic acid, thiol-)



Submitted by E. K. ELLINGBOE.¹

Checked by ARTHUR C. COPE and MALCOLM CHAMBERLAIN.

1. Procedure

Caution! All the steps of this procedure should be carried out under a hood because of the highly toxic nature of hydrogen sulfide and the probable toxicity and persistent unpleasant odor of thiolacetic acid.

A 200-ml. three-necked flask is fitted with a mercury-sealed glass stirrer, a reflux condenser, and a gas inlet tube and thermometer, both of which extend into the lower half of the flask. The top of the condenser is connected to a mercury bubbler tube, and the gas inlet tube is attached to the inlet tube of a gas-washing bottle which serves as a safety trap to prevent liquid from being drawn into the hydrogen sulfide source. The gas-washing bottle is connected through a drying tube containing anhydrous calcium sulfate (Drierite) to a T-tube. The vertical arm of the T-tube dips into mercury and forms a safety valve; the other arm is connected to a commercial cylinder (Note 1) or other source of hydrogen sulfide. To the flask are added 107 g. (100 ml., 1 mole) of 95% acetic anhydride and 1 g. (0.025 mole) of powdered sodium hydroxide. The assembly of the flask, condenser, inlet tube, and thermometer is weighed and arranged so that the amount of hydrogen sulfide introduced can be determined by subsequent weighing. The stirrer is started, and hydrogen sulfide is passed into the mixture as rapidly as possible without much loss of the gas through the bubbler connected to the top of the condenser. The temperature of the mixture rises to 55° within 30 minutes and is kept at 50–55° by intermittent cooling. The temperature begins to drop after 14–17 g. of hydrogen sulfide has been absorbed and is maintained at 50–55° by external heating. After a total reaction period of 6 hours, hydrogen sulfide ceases to be absorbed and the gain in weight amounts to about 31 g.

The reaction mixture is transferred to a 250-ml. Claisen flask (Note 2) and distilled rapidly at 200 mm. in order to separate the sodium salts (Note 3). The distillate of thiolacetic acid and acetic acid, b.p. 35–82°/200 mm., amounts to 120–124 g. It is fractionally distilled at atmospheric pressure through an effi-

cient, variable take-off type column ² with a 30- to 40-cm. section packed with glass helices. The fraction boiling at 86–88°, n_D^{25} 1.4612, is nearly pure thiolacetic acid and amounts to 55–57.5 g. (72–76%) based on the acetic anhydride (Notes 4 and 5). The residual liquid is mainly acetic acid. If distillation is continued after separation of the thiolacetic acid, the vapor temperature rises rapidly to the boiling point of acetic acid.

2. Notes

1. Cylinders of hydrogen sulfide are available from the Matheson Company, Inc., East Rutherford, New Jersey.

2. An all-glass distillation assembly equipped with ground joints is advisable because the hot vapor of thiolacetic acid rapidly softens rubber stoppers.

3. The product decomposes excessively if fractionation is attempted in the presence of the sodium salts. In larger-scale preparations the initial distillation should be conducted in small batches or, preferably, in a continuous stripping still.

4. Refractionation yields pure thiolacetic acid (with about 10% loss) with the following physical constants: b.p. 87°/760 mm., 50°/200 mm., 34°/100 mm.; n_D^{25} 1.4630; d_4^{25} 1.0634. Higher boiling points at atmospheric pressure have been reported: 88–91°, ³ 89°, ⁴ and 93°. ⁵

5. The submitters have prepared thiolacetic acid in yields of 65–70 g. (85–92%) by a similar procedure in which the reaction mixture is placed in the glass bottle (provided with a heating jacket and thermometer or thermocouple) of a low-pressure hydrogenation apparatus. ⁶ The mixture is shaken and hydrogen sulfide is introduced at 25–35 p.s.i., with repressuring to 35–40 p.s.i. whenever the pressure drops to 10 p.s.i. The heat of reaction raises the temperature to 60–65° in 12–15 minutes, after which the internal temperature is maintained at 60° by heating. Hydrogen sulfide absorption becomes negligible after 4 hours, and the mixture is allowed to cool while under pressure, vented, and the product is isolated in the manner described. The reaction also was conducted in a steel autoclave or hydrogen-

ation bomb at the full pressure of hydrogen sulfide in a commercial cylinder (about 300 p.s.i. at room temperature). Hydrogen sulfide poisons the ordinary hydrogenation catalysts, and low-pressure cylinders or hydrogenation bombs exposed to hydrogen sulfide may not be suitable for subsequent use in catalytic hydrogenations.

3. Methods of Preparation

Thiolacetic acid has been prepared from acetic acid and phosphorus pentasulfide;⁵ from acetyl chloride and potassium hydrosulfide;⁷ by the hydrolysis of diacetyl sulfide;⁸ from acetic anhydride and hydrogen sulfide;^{3,4,9} and from acetyl chloride and hydrogen sulfide in the presence of aluminum chloride.¹⁰ The procedure described⁹ differs from other procedures employing acetic anhydride and hydrogen sulfide^{3,4} most importantly in the use of alkaline rather than acidic catalysts, which the submitter found to cause slower absorption of hydrogen sulfide under pressure and to yield considerable diacetyl sulfide in addition to thiolacetic acid.

¹ E. I. du Pont de Nemours and Company, Inc., Wilmington, Delaware.

² *Org. Syntheses*, **25**, 2 (1935).

³ Clarke and Hartman, *J. Am. Chem. Soc.*, **46**, 1731 (1924).

⁴ Hands and Whitt, *J. Soc. Chem. Ind.*, **66**, 173 (1947).

⁵ Kekulé, *Ann.*, **90**, 309 (1854).

⁶ *Org. Syntheses* Coll. Vol. **1**, 66 (1941).

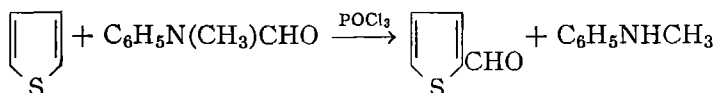
⁷ Jacquemin and Vosselmann, *Compt. rend.*, **49**, 371 (1859).

⁸ Davies, *Ber.*, **24**, 3551 (1891).

⁹ Ellingboe, U. S. pat. 2,412,036 [*C. A.*, **41**, 2074 (1947)].

¹⁰ Arndt and Bekir, *Ber.*, **63**, 2390 (1930).

2-THIOPHENECARBOXALDEHYDE



Submitted by ARTHUR W. WESTON and R. J. MICHAELS, JR.¹

Checked by CLIFF S. HAMILTON and JOE R. WILLARD.

1. Procedure

The reaction is carried out in a 500-ml. three-necked round-bottomed flask fitted with ground-glass joints and equipped with a thermometer, a mechanical stirrer, a dropping funnel, and a calcium chloride tube. In the flask are placed 135 g. (1.0 mole) of N-methylformanilide (Note 1) and 153 g. (91 ml., 1.0 mole) of phosphorus oxychloride, and the mixture is allowed to stand for 30 minutes (Note 2). Mechanical stirring is then begun, and the flask is immersed in a cold-water bath while 92.4 g. (1.1 moles) of thiophene is added at such a rate that the temperature is maintained at 25–35° (Note 3). After the addition is complete, the reaction mixture is stirred 2 hours longer at the same temperature and is then allowed to stand at room temperature for 15 hours. The dark, viscous solution is poured into a vigorously stirred mixture of 400 g. of cracked ice and 250 ml. of water. The aqueous layer is separated and extracted with three 300-ml. portions of ether. The ether extracts are combined with the organic layer and washed twice with 200-ml. portions of dilute hydrochloric acid (Note 4) to remove all traces of N-methylaniline (Note 5). These aqueous washings are in turn extracted with 200 ml. of ether, and the ether extract is added to the ether solution of the product. The combined ether extracts are washed twice with 200-ml. portions of saturated sodium bicarbonate solution (Note 6), then with 100 ml. of water, and finally are dried over anhydrous sodium sulfate. The yellow oil obtained by concentrating the ether solution is distilled from a 100-ml. flask fitted with a satisfactory column (Note 7). The yield of 2-thiophenecarboxaldehyde boiling at 97–100°/27 mm., n_D^{23} 1.5893, is 80–83 g. (71–74%). The product darkens on standing.

2. Notes

1. Directions for preparing this intermediate have been published earlier.²

2. The temperature of the mixture rises slowly to 40–45°, and a color change from yellow to red also occurs.

3. If the temperature is allowed to exceed 35° , a lower yield of aldehyde results.

4. This solution is prepared by mixing 50 g. of concentrated hydrochloric acid and 400 ml. of water. The aldehyde has appreciable solubility in strongly acidic solutions.

5. The original aqueous layer and the acidic extracts are combined, cooled, and made strongly alkaline with 450 ml. of 40% sodium hydroxide solution. The liberated N-methylaniline is extracted with three 200-ml. portions of ether. The ether extracts are combined, washed with 100 ml. of water, dried over anhydrous sodium sulfate, and concentrated. Distillation of the residue from a 200-ml. flask equipped with an 11-cm. Vigreux column gives 95.6 g. (89%) of N-methylaniline boiling at $96-100^{\circ}/27$ mm.; n_D^{23} 1.5717.

6. Care must be taken in adding the bicarbonate solution, as vigorous foaming occurs until neutralization is complete.

7. The submitters used an 11-cm. Vigreux column; the checkers employed a 10-in. column of the same type.

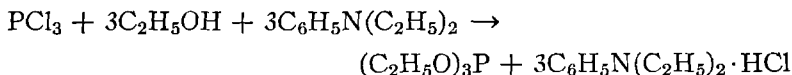
3. Methods of Preparation

The present procedure is a modification of a previously described method.^{3,4} 2-Thiophenecarboxaldehyde has been obtained by the hydrolysis of 2-thienylmethylhexamethylenetetrammonium chloride; ^{5,6} by the Rosenmund reduction of 2-thiophenecarboxylic acid chloride; ⁷ by the decarboxylation of 2-thienylglyoxylic acid; ⁸ by the Gattermann reaction with thiophene; ⁹ by hydrolysis of the acetal obtained by the action of 2-thienylmagnesium iodide on ethyl orthoformate; ⁸ by the oxidation of 2-thenyl alcohol; ¹⁰ by the hydrolytic cleavage of N-(2-thenyl)-2'-thenaldimine; ¹¹ by treatment of N-2-thenylformaldimine with ammonium chloride and formaldehyde; ¹² and by the action of 2-thienylmagnesium bromide on ethyl formate.¹³

- ¹ The Abbott Laboratories, North Chicago, Illinois.
² *Org. Syntheses*, **20**, 66 (1940).
³ King and Nord, *J. Org. Chem.*, **13**, 635 (1948).
⁴ Weston and Michaels, *J. Am. Chem. Soc.*, **72**, 1422 (1950).
⁵ Dunn, Waugh, and Dittmer, *J. Am. Chem. Soc.*, **68**, 2118 (1946).
⁶ *Org. Syntheses*, **29**, 87 (1949).
⁷ Barger and Easson, *J. Chem. Soc.*, **1938**, 2100.
⁸ du Vigneaud, McKennis, Simmonds, Dittmer, and Brown, *J. Biol. Chem.*, **159**, 385 (1945).
⁹ Reichstein, *Helv. Chim. Acta*, **13**, 355 (1930).
¹⁰ Emerson and Patrick, *J. Org. Chem.*, **14**, 790 (1949).
¹¹ Hartough, *J. Am. Chem. Soc.*, **69**, 1355 (1947).
¹² Hartough, Meisel, Koft, and Schick, *J. Am. Chem. Soc.*, **70**, 4013 (1948).
¹³ Gattermann, *Ann.*, **393**, 215 (1912).

TRIETHYL PHOSPHITE

(Ethyl phosphite)



Submitted by A. H. FORD-MOORE and B. J. PERRY.¹

Checked by WILLIAM S. JOHNSON and JAMES ACKERMAN.

1. Procedure

A solution of 138 g. (175 ml., 3 moles) of absolute ethanol (Note 1) and 447 g. (477 ml., 3 moles) of freshly distilled diethylaniline in 1 l. of dry petroleum ether (b.p. 40-60°) is placed in a 3-l. three-necked flask fitted with a sealed stirrer, an efficient reflux condenser, and a 500-ml. dropping funnel (Note 2) which is charged with a solution of 137.5 g. (87.5 ml., 1 mole) of freshly distilled phosphorus trichloride in 400 ml. of dry petroleum ether (b.p. 40-60°). The flask is cooled in a cold-water bath. With vigorous stirring (Note 3), the phosphorus trichloride solution is introduced at such a rate that the mixture boils gently towards the end of the addition. After the addition, which requires about 30 minutes, the mixture is heated under gentle reflux for about 1 hour with stirring. The suspension, containing a copious pre-

cipitate of diethylaniline hydrochloride, is then cooled and filtered with suction through a sintered-glass funnel. The cake of the amine salt is well compressed and washed with five 100-ml. portions of dry petroleum ether (b.p. 40–60°). The filtrate and washings are combined and concentrated by distillation at water-bath temperature through a 75-cm. Vigreux column. The residue is transferred to a pear-shaped flask and distilled under water-pump vacuum through a 75-cm. Vigreux column. After a small fore-run, the product is collected at 57–58°/16 mm. (51–52°/13 mm., 43–44°/10 mm.). The yield of colorless product is 138 g. (83%), n_D^{25} 1.4104–1.4106, d_4^{20} 0.963 (Notes 4 and 5).

2. Notes

1. It is important that the ethanol be thoroughly anhydrous. The checkers employed ethanol dried over magnesium ethoxide.²

2. It is convenient to connect the dropping funnel to the flask by a piece of 20-mm. glass tubing about 10 cm. long which is sleeved into the neck of the flask by a section of rubber tubing. By this means, the rate of introduction of the phosphorus trichloride solution may be readily observed and clogging by the copious precipitate of diethylaniline hydrochloride is obviated.

3. If efficient mixing is not obtained, hydrogen chloride may be liberated locally and one of the ethyl groups eliminated as ethyl chloride with the resulting appearance of diethyl hydrogen phosphite in the final distillate.

4. The recovered petroleum ether and fore-run contain some of the product. By using the recovered petroleum ether in subsequent runs and adding the fore-run before the final distillation, the yield is increased to 86–90%.

5. Triisopropyl phosphite is prepared similarly, using anhydrous isopropyl alcohol in place of ethanol. It has the following properties: b.p. 43.5°/1.0 mm.; n_D^{25} 1.4080; d_4^{17} 0.917.

3. Methods of Preparation

The method described here is essentially that of McCombie, Saunders, and Stacey ³ except that diethylaniline is employed in place of dimethylaniline or pyridine. Diethylaniline has the advantage that the hydrochloride formed in the reaction is very easily filtered and is non-hygroscopic.

¹ Chemical Defence Experimental Station, Porton, Nr. Salisbury, Wilts, England.

² Fieser, *Experiments in Organic Chemistry*, 2nd ed., p. 359, D. C. Heath and Company, Boston, Massachusetts, 1941.

³ McCombie, Saunders, and Stacey, *J. Chem. Soc.*, **1945**, 381.

SUBJECT INDEX

(This cumulative index comprises material from Volumes 30 and 31; for previous volumes see Collective Volumes 1 and 2 and Volume 29)

Names in small capital letters refer to the titles of individual preparations. A number in ordinary bold-face type denotes the volume. A page number in bold-face italics indicates that the detailed preparative directions are given or referred to, entries so treated include principal products and major by-products, special reagents or intermediates (which may or may not be isolated), compounds mentioned in the text or Notes as having been prepared by the method given, and apparatus described in detail or illustrated by a figure. Page numbers in ordinary type indicate pages on which a compound or subject is mentioned in connection with other preparations. For example, Allylbenzene, **31**, 85, **86**, indicates that allylbenzene is mentioned on page 85, and that directions for its preparation are given on page 86, of Volume 31.

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NOMENCLATURE

Preparations appear in the alphabetical order of common names of the compounds. For convenience in surveying the literature concerning any preparation through *Chemical Abstracts* subject indexes, the *Chemical Abstracts* indexing name for each compound is given as a subtitle if it differs from the common name used as the title.

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